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POLIOMYELITIS IN THE ARCTIC*

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DURING the autumn of 1948 and the winter of 1949 a widespread epidemic of acute anterior poliomyelitis occurred in the Eastern Arctic of Canada. This epidemic has attracted much attention since it was at its height during the winter in an isolated district, sparsely settled by Eskimos who had previously had no poliomyelitis. Thorough investigation was undertaken by Indian Health Services in the Federal Department of Health and Welfare, to whom this report is accordingly submitted.

Two trips in ski-equipped aircraft were arranged by the Royal Canadian Air Force, the first in the first week of March and the second in the first week of May. The party received most valuable assistance from members of the white settlement at Chesterfield. Without their general knowledge of the Eskimo and familiarity with local conditions the important features of the epidemic could not have been discovered.

THE LOCALE

Reference to the map will show the area affected to be between 60 and 65° N. and between 90 and 100° W. Chesterfield Inlet is a thousand air miles north of Winnipeg. This is one of the most northerly epidemics of poliomyelitis on record and among the very few known to have occurred in Eskimos. Arne Hoygaard[1] refers to an epidemic in August-November, 1925, at Angmagssalik, East Greenland (65° N.) which caused 27 deaths among 800 Eskimos. He also refers to a report of an epidemic in West Greenland by A. Bertelson[2] in 1935.

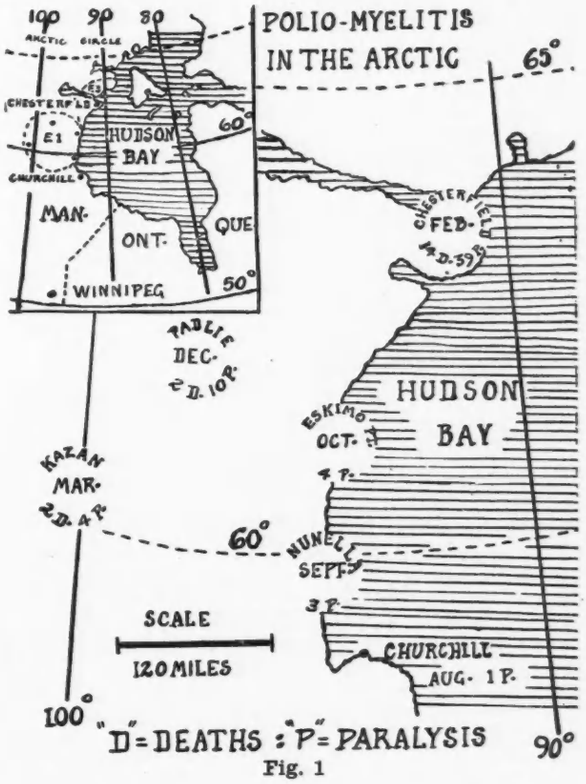

Fig. 1

It will be seen that the epidemic occurred during the coldest part of an unusually cold

* This study was conducted under the direction of the Department of National Health and Welfare.

winter. The frigidity is much increased by almost constant wind. As measured by "wind chill", it is said that this particular region is as cold as any on the Arctic mainland. Precipitation amounts to about 10 inches a year. This accumulates as ice and snow for about 9 months of the year. The question of insect vectors (except lice) in this epidemic would seem to be out of the question.

DEMOGRAPHY

There are about 500 Eskimos trading into the posts at Nunella, Eskimo Point, Padlei and Kazan. There are 275 (66 families) trading into Chesterfield. These two districts are officially designated Eastern 1 and Eastern 3 and will hereafter be referred to as E.1 and E.3.

METEOROLOGICAL DATA

THE TEMPERATURE READINGS AT CHESTERFIELD INLET ARE GIVEN BELOW

	High temperature	*Low temperature*	*Mean temperature*
1948			
January	17°	–48°	–23°
February	5°	–47°	–31°
March	16°	–46°	–21°
April	32°	–32°	– 2°
May	38°	– 6°	20°
June	57°	27°	38°
July	68°	35°	50°
August	86°	35°	52°
September	52°	27°	42°
October	45°	– 3°	26°
November	34°	–19°	10°
December	27°	–38°	–14°
1949			
January	6°	–48°	–29°
February	–21°F.	–49°F.	–38°F.

Only a few natives have a fixed abode; these live at the various posts as employees of the North West Mounted Police, the Missions and the Hudson's Bay Company. The other families are nomadic, but as a rule cover a radius of only about 100 miles in their travels. They live in groups of a few families which are usually related, sometimes in a patriarchal pattern. The groups commonly consist of 10 to 50 individuals. The contact between individuals of each group is very intimate. In contrast, the contact between districts is infrequent. For example, those at Chesterfield rarely meet those to the south or further north. Indirect contact is made along the coast each summer (July to September) through the medium of several supply ships.

The primitive Eskimo in this region lived entirely on the spoils of hunting and fishing. His clothes came from caribou skins and his food from caribou, seal, walrus and fish. The only objects of barter with traders were fox skins and a few other pelts. With these he purchased ammunition, tea, tobacco and some minor luxuries such as biscuits, flour and canned goods. Several times a year he made a trip to the nearest post and then returned "to the land" for caribou, fish and fox or "to the flow edge" for seals, walrus or bear. Those who were farther south derived comparatively little from the Bay and were not interested in seal hunting, while those in the north depended more on the sea. During the nine months of winter they travelled along their trap lines and on hunting expeditions by dog teams.

This primitive life has been modified in recent years by several circumstances. The Federal family allowance has conferred relative wealth on many families. Credits have accumulated while the plan has been put into gear, so that most families have several hundred dollars at their disposal. This may be drawn in the form of certain staple foods and ammunition. The urgent necessity of hunting to preserve life has been removed. Very few natives look beyond the present and the idea of securing the future rarely disturbs their equanimity. The government also has been quite liberal in supplying "destitute allowance" for the disabled, orphans, widows and improvident. In recent years foxes have been scarce and the price has been poor; this has increased the dependence of the poorer class of native. As a result of these circumstances, there has been a definite tendency for natives to come to the post more frequently and remain longer. Efforts to discourage this tendency to "hang about" the posts are made by the traders and by the police and have been fairly successful in the southern regions but less so in Chesterfield. It will be seen that the explosive nature of the epidemic at Chesterfield was largely due to the concentration of native population about this point.

HABITS AND HYGIENE

In the winter the natives live in igloos which are rapidly constructed as occasion demands. These snow houses are invariably small, crowded, very cold and grossly unsanitary. All the inmates sleep on a common snow bench, bundled under caribou skins; little attention is given to the disposal of excreta which is sometimes deposited in the ante-chamber; nasal discharge and chronic coughing and spitting is almost universal. In the three months of sum-

mer caribou-hide tents are substituted for igloos; these are no improvement on the snow house from the hygienic point of view. Personal hygiene and washing is almost unknown and little effort is made to cleanse cooking utensils or the drinking cups. Evidence of tuberculosis is widespread; purulent nasal discharge is very common among the children and pyogenic skin infection is often seen.

The eating habits of the Eskimo are irregular, with a minimal amount of preparation and cooking. The food consists chiefly of raw caribou, seal meat, sun-dried fish, bannock, hard biscuits, and some lard, jam, dried milk, and a few other items. He consumes large quantities of tea which he drinks several times a day. He kills whatever game is available and may cache this food (caribou) in a frozen state for future use; he has little regard for its state of preservation and in fact seems to prefer it "high". It is not uncommon for Eskimos to gorge while the food is plentiful and to go on reduced quantities at other times. Babies are nursed by the mother until two or three years of age, or until another child is born. Generally speaking, the Eskimo feeds his children first with the choicest cuts of meat. Mothers frequently chew meat before placing it in the child's mouth.

EPIDEMIOLOGY

The first outbreak. — In order to follow the course of the whole epidemic in the Eastern Arctic it is necessary to divide it into two separate outbreaks, which show marked contrasts. The first took place in District E.1, *i.e.*, Nunella, Eskimo Point, Padlei and Kazan. Map No. 1 shows the geographical relationship of these posts to one another and also indicates the time of infection and the number of deaths and paralytic cases at each point. The cases recorded on the map are all well authenticated, most of them having been examined by medical men. The incidence of non-paralytic cases cannot be stated precisely because of the difficulty in procuring dependable histories. The Eskimo has much difficulty in describing anything that took place more than a few days in the past. In his efforts to recollect the recent past he lapses into profound thought, breaks into a profuse sweat and has recourse to much manipulation of digits. When he ultimately emerges with a smile and an answer one feels that he has no confidence whatever in his result. Experience has shown that he is justified; his histories rarely correspond chronologically or otherwise with what is known to have occurred. For this reason no figures on total incidence can be given. Non-paralytic or abortive cases were common and many were examined. From the stories as given by the natives one got the impression that in some camps and in some families every one except the babies had symptoms.

The total morbidity and mortality with percentage of population involved for the minor and the major attacks are shown in Table I. In comparison with other epidemics this shows an unprecedented attack and mortality rate.

The source of the infection was no doubt from Churchill. During the summer of 1948 several hundred workmen were employed at this port at which there is a military installation and some troops. On July 8, 1948, a member of the R.C.A.F. was flown to Winnipeg where the diagnosis of poliomyelitis was confirmed. The first Eskimo cases appeared in Nunella, 75 miles north of Churchill, in September. There were no deaths, but three young adults (2 male and 1 female) in a group of 20 have residual paralysis. The worst case among these was evacuated by boat on September 28 and was ultimately treated in the Winnipeg General Hospital where he was found to have a typical moderately severe paralysis of the left lower limb and a high spinal fluid protein.

TABLE I.
TOTAL MORTALITY AND MORBIDITY

	Deaths	*% of Pop.*	*Para.*	*% of Pop.*
E.1	4	0.8	21	4.2
E.3	14	5.1	39	14.0
Total	18	2.3	60	7.7

The spread from Churchill to Nunella could have been through one of several channels since occasional summer boats touch at both points. One Eskimo ("Tutu"), who is not known to have been infected, left Churchill on September 13, 1948, for his home north of Eskimo Point. On his way he visited at Nunella, Eskimo Point and several other camps and no doubt lived in the tents with his friends.

The epidemic appeared at Eskimo Point, 100 miles north of Nunella, early in October, carried there either by "Tutu" or by boat crews. Eight cases are said to have occurred in the district and five cases of paralysis resulted,

four among natives and one in an Anglican missionary. This solitary case in the white population is not included in our figures. All of the other paralysis cases have been examined and show typical involvement.

Between December 5 and 15 one of the Eskimo Point cases who had residual paralysis of the shoulder girdle visited all the camps in the Padlei areas (125 miles inland). About two weeks after his departure from the district, cases began to appear. In a group of 50 natives there were 2 deaths and 10 cases with paralysis. Two of these have since been admitted to hospital in Winnipeg with severe paralysis.

On February 1 two natives from a group of 48 in Kazan Camp, (150 miles S.W.), visited Padlei. They returned to Kazan on February 27 bringing two other Eskimos with them. Within a week two natives who had not left the camp became ill and ultimately there were two deaths and four cases of paralysis.

The spread of this lesser epidemic appears to be clear. It is not known how many natives were actually ill but the report on deaths and paralysis has been checked by the police during patrols and by Dr. Moody, and may be regarded as accurate. In the whole district (500 natives) there were 4 deaths and 21 cases of known paralysis. The general pattern and the extent of this minor outbreak conforms fairly well to what is expected in white communities. It will be seen to contrast very strikingly with what took place in the second outbreak at Chesterfield.

Second outbreak (Chesterfield Inlet).—The first case appeared here on February 14, 1949, and the last on March 7. There were 14 deaths (from February 20 to March 2) and 39 cases were paralyzed. Since there were only 275 Eskimos in the area this represents a mortality rate of over 5%, a paralysis rate of over 14% of the whole population. The total morbidity rate is not known, but all the evidence suggests that at least 50% of the total native population had symptoms.

The enormity of this outbreak can be appreciated only if one translates the death and disability rates into the corresponding figures in a large city. For example: if an epidemic of the same destructiveness were to attack Greater Winnipeg (300,000), more than 50% of the people would be laid up, there would be in the course of 10 days 15,000 deaths and 42,500 people would be left with paralysis.

The only known contact with the minor epidemic in the more southerly district was through a missionary who arrived at Chesterfield from Eskimo Point on January 28, 1949. He was not examined and is not known to have been ill. He had had close contact with Eskimos in the E.1 district and on going to Chesterfield he was housed in the Mission and associated with the natives in the hospital and with others then congregated at the post. The first case was discovered 16 days after his arrival. The onset dates of 51 of these cases and the dates of deaths are shown in Table II.

Except for the times of death (which were taken from official death certificates) the dates given in the table are approximations. No one could be more indifferent to the passage of time or more vague in temporal orientation than the Eskimo.

TABLE II.

	February															*March*							
	14	*15*	*16*	*17*	*18*	*19*	*20*	*21*	*22*	*23*	*24*	*25*	*26*	*27*	*28*	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*Total*
Onset	3	1	2	7	3	1	8	4	1	2	2	2	4	1	2	2	3	–	–	–	1	2	51
Death							1	2	1	1	1	3		3			2						14

The whole epidemic lasted only from February 14 to March 7 (21 days) and all the deaths occurred in a period of 11 days (February 20 to March 2). Of the 14 deaths, 3 were in the hospital (for other reasons), and 7 others were living on the settlement when the epidemic started. The routes by which the other four were infected are of interest. The dates in this instance are accurate, having been recorded by the police at the time.

CASE 1

Akearok, a male aged 10, lived with his family 35 miles from Chesterfield. This family had had no contact with any other natives for some months. His father visited the settlement and received family allowance on February 11, returning home on the following day. On February 22, Akearok died in his father's igloo with paralysis.

CASE 2

Kau (female, aged 11) and Igviksak (female, aged 14) lived up the Inlet, 15 miles from the settlement. Frequent visits to Chesterfield by various individuals in the camp and possibly by the patients had been made. On February 23 (9 days after the first case) Kau died in camp. Soon after, on the 25th, Igvigsak was brought

into the hospital with widespread paralysis and died on February 27.

CASE 3

Kappi, male 33, lived in a camp with 20 others, 50 miles north of Chesterfield. There had been no contact with any other camp for some months. Keelak (his brother) and Akralayuk (a male relative, aged 26) left the camp on February 10 and visited in Chesterfield. They left on their return journey on February 13, just before the first cases were discovered. Kappi died on March 2 with paralysis, not more than 15 days after the infection was first brought to the camp. Akralayuk developed paralysis after return to camp and almost all of the other members of the group had symptoms, four of whom now have residual paralysis.

It will be seen from the above evidence that this epidemic spread rapidly through the whole community like an acute and highly infectious fever, quite unlike the usual course of poliomyelitis in white communities. The incubation period appears to have been short and the course very brief in the fatal cases. In 11 of the fatal cases, in which the Eskimo history sounded plausible, the times between onset of symptoms and death were 5, 4, 4, 12, 6, 5, 4, 6, 4, 4, and 5 days. It seems likely that these histories date from the beginning of the paralysis and not from the primary invasion which is commonly several days earlier and sometimes so mild as to be disregarded.

The explosiveness and devastation of the Chesterfield attack is unprecedented. The circumstances that may have contributed to its violence and which account for the contrast to the lesser attack in E.1 may be considered. (1) Being farther north and much less in contact with white people the natives at Chesterfield may have a lower resistance. (2) The winter season involves crowding into camps and in igloos, less ventilation and long hours of intimate contact. (3) Perhaps the chief cause of the rapid spread in Chesterfield is the great tendency of natives to congregate about the Post, the Mission and the hospital. At the time of the outbreak there were about 120 natives on the settlements (25 in hospital, 32 employed, 14 destitute and on relief, 49 squatters or floaters). Most of the others were within a short distance of the post and had frequent contact. The further accumulation caused by the epidemic itself fed the flame. On May 1, 1949, when the district was last visited almost 200 of the total population were living within 10 miles of the post.

AGE AND SEX INCIDENCE

Table III shows the number of those in each age and sex group who were paralyzed or died. This includes both the minor and major epidemics. In 7 of the total of 78 cases the age and sex were not recorded.

The ages at death were: 8, 10, 10, 11, 14, 18, 19, 31, 33, 47, 49, 56, 59 and 64. It will be observed that there was no death under the age of 8; otherwise there is equal age distribution.

There will be seen to be a definite preponderance of males. This is partly accounted for by the fact that 53.5% of the population are male. The deaths showed an equal sex distribution (seven males and seven females).

There was no case under the age of 3. Thereafter the age distribution was fairly even. Table IV shows the percentage infected in each age group in the Chesterfield outbreak. The number of natives in each group as at December, 1948 is shown. Among the cases, a few are included who survived and had no residual paralysis; these were all seen by medical men who considered the diagnosis incontrovertible.

These figures show a marked tendency to even distribution through all groups except in those under four. This is in striking contrast to what is usually found in epidemics among

TABLE III.

Age	*3 to 4*	*5 to 9*	*10 to 14*	*15 to 19*	*20 to 24*	*25 to 29*	*30 to 34*	*35 to 39*	*40 to 44*	*45 to 49*	*50 to 54*	*55 to 59*	*60 +*	*Total*
Male	1	10	5	6	5	2	6	2	1	2	0	2	2	44
Female	1	5	4	3	5	2	3	0	0	1	0	0	3	27
Total	2	15	9	9	10	4	9	2	1	3	0	2	5	71

TABLE IV.

Age	*0–4*	*5–9*	*10–14*	*15–19*	*20–24*	*25–29*	*30–34*	*35–39*	*40–44*	*45–49*	*50–54*	*55–59*	*60+*
Census	53	56	33	26	18	12	24	9	10	9	4	8	13
Cases	2	13	8	11	4	2	6	1	2	3	—	2	3
Percent	4	23	25	42	22	16	25	11	20	33	0	25	23

white people. It suggests an absence of immunity in the whole population, except in babyhood, and to a lesser extent in the three and four age groups.

The portal of entry could have been in the respiratory or the gastro-intestinal tract. Insanitation and intimate contact provided excellent opportunities for both. The very rapid spread and short course might be used as an argument for the respiratory route. The fact that the brunt of the disease fell on the lower cord and also the fact that babies escaped might suggest intestinal infection. But any one of these circumstances might depend on the peculiar susceptibility of the hosts. No insect vector — except the louse — could possibly be incriminated under the circumstances.

It has often been noted that multiple family cases are rare in poliomyelitis. An analysis of 25 families in the Chesterfield attack (Table V)

TABLE V.

NUMBER OF FAMILIES HAVING ONE TO SIX CASES

Number of cases in family	*Number of families*	*Percentage of total*
1	6	24
2	4	16
3	4	16
4	2	8
5	0	0
6	2	8
No cases	7	28
Total....	25	100%

shows no such limitation. Twelve of the 25 families had more than one case and in each of two families there were six cases.

QUARANTINE

As soon as the clinical diagnosis of poliomyelitis was made the district was quarantined and every effort has been made to prevent any contact with natives in contiguous districts. The question as to the duration of quarantine is important. In the usual epidemic of poliomyelitis in regions well populated by white people, isolation and quarantine are rarely seriously attempted and commonly thought to have little effect; experience suggests that under these circumstances the disease is transmitted only after most intimate contact. Such a casual attitude is evidently not justified when dealing with this infection among Eskimos. One cannot escape the conviction that spread of the virus to similar Eskimo communities will cause comparable damage. In July when the ice and snow melt, the whole environment of Chesterfield will be heavily contaminated and no doubt many of the Eskimos will be carriers. If the boat traffic is allowed to operate in the usual way there will be intimate contact with boat crews and there will be real danger of carrying the virus to Baker Lake and to northern posts along the coast, especially to Repulse Bay. Since the hazard to the life of the Eskimo is so great, maintenance of the quarantine has been extended till after the navigation season. This will not prevent ships from leaving supplies. It will demand a careful vigil to prevent contact between the crews and the natives.

CLINICAL FEATURES

The onset was fairly typical of acute poliomyelitis. Fever, headache and anorexia were invariable. There was more gastro-intestinal disturbance than is usual; many cases started with vomiting and a few had diarrhœa. This "invasion" period lasted for 2 or 3 days and was followed by complete recovery in the majority of cases. This so-called "abortive poliomyelitis" is by far the commonest type of case seen in any epidemic. It, indeed, should be regarded as the disease proper; paralysis is merely a complication. The actual severity of any epidemic depends on what proportion of these go on to the paralytic stage. It is of interest that of the six white children in the community, four had an attack of this sort and none developed the secondary attack with paralysis. All of these children (except one infant) have spent the greater part of their lives in white urban communities. Of the 19 white adults two had minor complaints that could have been due to the virus. This conforms to the usual course during epidemics among urban white populations.

The paralytic stage followed after an interval of two or three days of comparative well being during which time many of the Eskimos returned to their usual activities. The second attack came on suddenly with headache and pain in muscles and was followed by muscle weakness and spasm.

The demonstration of a pre-paralytic and a paralytic attack was not possible in all cases. In some cases the primary attack was so mild as to be overlooked and in some the whole history was so vague as to be inconclusive. It so happened that of 25 patients who were in the Sisters' Hospital when the epidemic broke out,

13 developed symptoms; three of these died and seven others developed paralysis. Two of these latter were having night and morning temperature recordings for other reasons and both showed the typical pre-paralytic episode. One of these charts is reproduced below (Fig. 2).

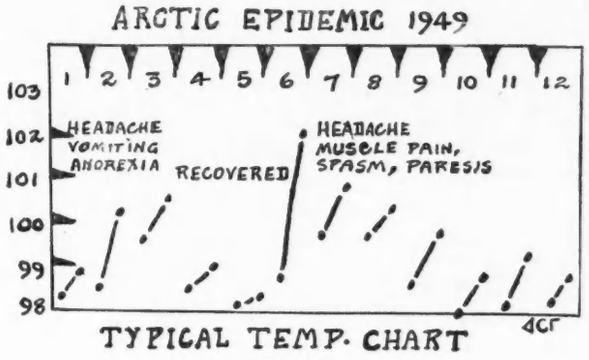

Fig. 2

Distribution of paresis in 50 cases that were examined on several occasions was as follows:

Trunk	24
Left lower limb	32
Right lower limb	31
Left upper limb	23
Right upper limb	10
Bladder	2
Right diaphragm	2

From this it is evident that the brunt of the attack was on the dorsal and lumbar cord. Abdominal and spinal muscles were involved in nearly half of the cases. One or both lower limbs were involved in all but six cases. The upper limbs were much less frequently affected and a most striking feature was the selection of the left arm, it being involved in 23 cases as against only 10 cases on the right. There were two cases of bladder paralysis in youths. These recovered in a few days. There were also two cases of paralysis of the right diaphragm, both of which are improving.

This distribution of paralysis is in strong contrast to what is commonly found in epidemics among white people.[3] There were very few signs of meningeal, bulbar or cerebral involvement and the neck muscles were not much affected. There was no cranial nerve involvement. This tendency to select the lower cord suggests that infection was introduced by the gastro-intestinal rather than the respiratory tract.

From the descriptions of the symptoms of those who died, given by Dr. Moody and the Sisters, it was evident that death was caused by a gradually ascending paralysis. The lower limbs were first involved, then the arms and finally the respiratory muscles. Respiratory distress and cyanosis were noted for only a short time before death; there was no difficulty in swallowing or phonation and consciousness was retained.

The principal disability will arise from paresis of trunk muscles, with effect on the spine and abdomen. This localization produced a remarkable posture during the acute stage; many of the patients were found to be lying with the spine fixed in lordosis, quite unable to flex and with much loss of tone in the abdominal muscles. Attempt at flexion met with resistance, but no complaint of pain except in the hamstrings.

The spinal fluid findings were typical. Most cases had the first puncture several days after onset so that nearly all the cells were lymphocytes. No correlation was found between the cell count and the paralysis. The highest count was in a 31-year old pregnant woman who on the fifth day of her illness showed a total count of 254 (172 lymphocytes) and only slight evidence of paralysis. In contrast a 15-year old boy who had gross and widespread paralysis showed only 10 cells on the tenth day of his illness.

In general the cell counts were felt to be lower than is usually seen. Unfortunately only seven counts were done during the first week. The total cells were: 160, 150, 9, 258, 6, 50, 66. Since these were all badly paralyzed cases, these figures again demonstrate the lack of relationship between total cell count and the degree of paralysis. The total cerebrospinal protein showed a consistent elevation in all of the 12 paralyzed cases in which it was followed. Table VI shows the cell counts and the total protein at 10 day intervals in these patients.

It will be seen that the total protein rose, in each case, as the cells disappeared. The peak of the rise on the average is seen between the 20th and 30th day of the illness. In 7 of the cases a level had fallen to 55 or less between the 30th and 50th days. Two cases still showed abnormal levels (120 and 110) between the 70th and 80th days. The height of the protein level does not indicate the degree of paralysis or the progress of the case accurately, though there is a rough correlation.

TABLE VI.

CEREBROSPINAL FLUID CELLS AND PROTEIN (CELLS/PROTEIN) IN 12 PARALYZED CASES

	Days								
Cases	*0–9*	*10–19*	*20–29*	*30–39*	*40–49*	*50–59*	*60–69*	*70–79*	*80–89*
1		20/170	0/300		0/240			0/120	
2		48/110	12/150	10/140	5/80				5/60
3	150/40	12/110		1/190				2/110	
4		10/65	21/160	2/150	0/50				
5	9/45	3/80	5/150	0/55					
6		45/65	10/85	6/65	2/55				
7	59/40	20/75	7/120		4/75			4/50	
8	6/55	2/120	4/75		1/50				
9	10/45	5/90	3/65		2/40				
10		13/95	7/90	2/90	3/50				
11		42/100	29/140	3/90	4/90				0/55
12		6/65	14/90	2/55					
Average..	47/45	20/90	9/130	3/104	2/81				

ANTHROPOMORPHIC FEATURES

Many observers have pointed out that white children susceptible to poliomyelitis conform to a specific and recognizable type. Draper[4, 5] has made an exhaustive study of this subject. Among the features that characterize the type are the following: pigmented spots on skin; irregularity and spacing of teeth; large central incisors; mongoloid eyes; broad short hands; relatively broad pelvis; widely spaced eyes.

Though no specific anthropometric observations were made on the group under discussion, it is well known that most Eskimos show all of these characteristics.

In connection with the distribution of paralysis Draper's observation is also of interest:

> "In the children stricken under seven years of age there is a tendency for the possessors of five and six characters to be paralyzed in the lower extremities with much greater frequency than in other parts of the body. On the other hand, those individuals maimed after seven years of age and who possess fewer of the six characters display a greater trend toward upper extremity and more general involvement."

The abnormal susceptibility of the Eskimo and the distribution of the paralysis both give surprising support to Draper's thesis. Further anthropological studies on Eskimos would be justified.

TREATMENT

Fortunately, at Chesterfield, there is a small, well-equipped hospital in charge of the Sisters of Charity (Grey Nuns) of Montreal. Its 25 beds were soon overflowing, in spite of which satisfactory general care was given to all those patients who could be brought in. The more severe cases (22 in all) were flown to Winnipeg where they received physiotherapy in the King George Municipal Hospital. In May a trained physiotherapist was flown into Chesterfield where the minor cases were treated.

AUTOPSY FINDINGS

Two autopsies were performed at Chesterfield Inlet; both had presented symptoms similar to many of the non-fatal cases. The first was performed on a male, 60 years of age, who died on March 3, 1949, after an illness of about five days. The course of his disease was characterized by headache, pain in the lumbar region and an ascending type of paralysis involving first the legs, then the back and arms.

The post mortem examination, conducted within an hour of death, supplied excellent material for histologic study. The body length was about 155 cm. Although the age was given as 60 years he appeared to be at least 10 years older. The body build was sthenic in type, the chest showing a marked increase in anteroposterior diameter.

The viscera of the thorax and abdomen showed no gross abnormalities, changes being confined to the central nervous system, particularly the spinal cord. The vessels of the meninges and surface of the cord were dilated. The anterior and posterior horns and the commissure were pink, soft and protruded from the cut surface in an "H" shape. This was most marked in the lumbar region, but present in the cervical cord to a lesser degree. The superficial vessels of the brain were congested and the gyri showed considerable flattening. The white matter showed some congestion throughout. Microsections of the spinal cord were truly striking, particularly in the lumbar region, with a decreasing degree of severity at higher levels, although changes were seen as high as the basal ganglia.

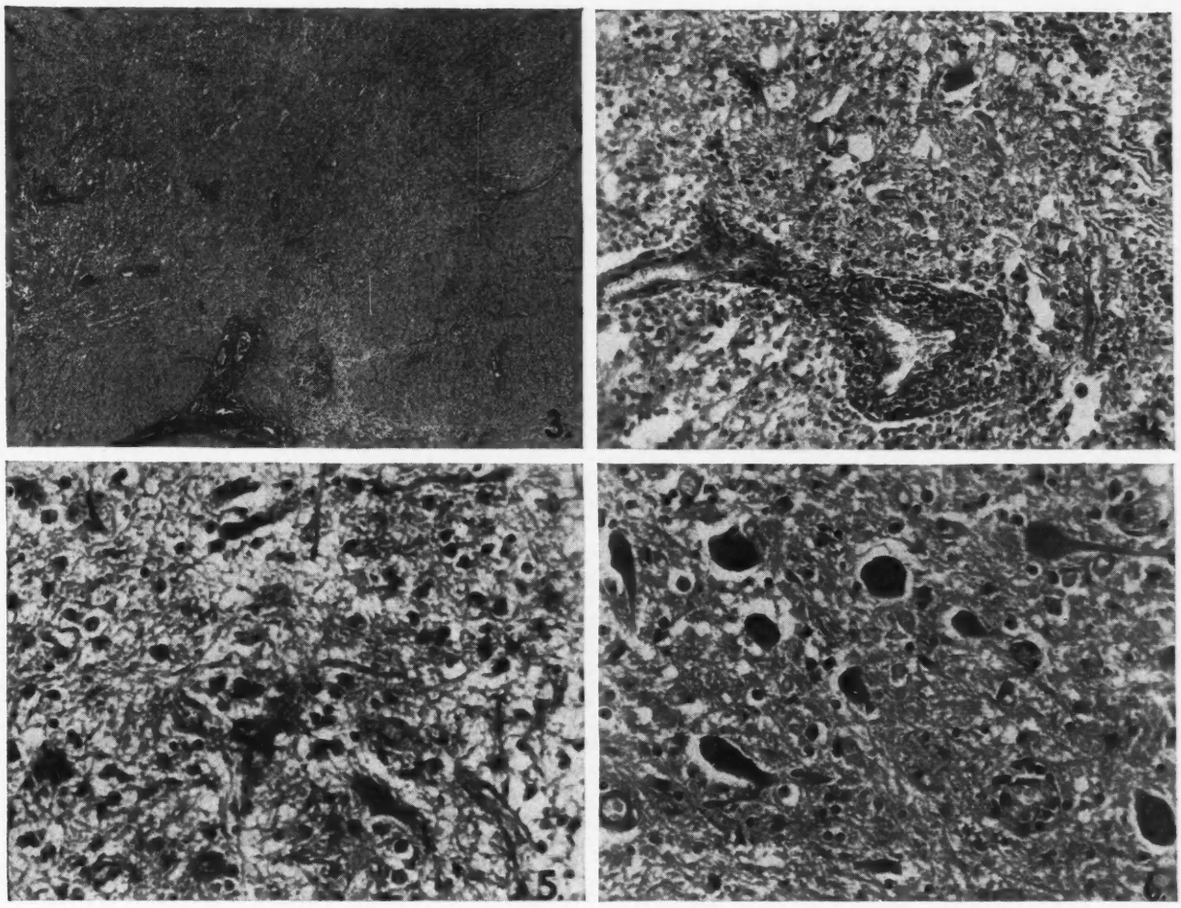

Fig. 3.—Lumbar cord x 19. At the lower centre is the central canal. To the left of this is the anterior fissure showing subarachnoid perivascular round cell infiltrations. The periphery of the cord is seen in the upper left corner. The small artery seen in the centre left is the centre of Fig. 4. **Fig. 4.**—Lumbar cord x 130. Lower left shows a branch of the anterior spinal artery with perivascular round cells. At upper centre right is the remains of a neuron cell showing advanced chromatolysis. Interstitial vacuolization is marked. **Fig. 5.**—Lumbar cord, central portion of the anterior horn x 300. There are scattered remains of neuron cells as small smudges. Glial cell cytoplasm is swollen; some interstitial œdema is seen. **Fig. 6.**—Thoracic cord, the posterior part of the anterior horn x 350. Neuron cells are shrunken, distorted and hyperchromatic. Remains of nucleus may be seen in some.

The accompanying photomicrographs reveal the extent of the lesions in the brain and spinal cord in this case.

Conclusion:—Poliomyelitis.

The second autopsy was on a male, 17 years of age, who died February 25, 1949, about a week before our arrival. During this time the body was frozen at about –40° F. It was partially thawed, but became frozen a second time and was again partially thawed for autopsy. Due to ice crystal formation and autolysis the tissue was of little use for histological study, but the grey matter of the cord was grossly similar to the first case. On section we were able to detect one perivascular collection of round cells in the anterior horn and suggest that the disease process was similar to the previous case.

Tissue was saved for virus studies from the cerebral cortex, basal ganglia, medulla, dentate nucleus and three levels of the spinal cord. These were sent to the Connaught Laboratory and suspensions were injected into monkeys. The animals that developed paralysis were autopsied and showed the lesions of poliomyelitis.

VIRUS STUDIES

Various materials (brain, cord, throat washings and fæces) were collected and forwarded to the Virus Laboratories in Ottawa and to the Connaught Research Medical Laboratory. Some samples of each of these have produced positive results after monkey inoculation. These studies will be the subject of a separate report.

SUMMARY

1. A widespread epidemic of acute poliomyelitis is described among Eskimos in the Eastern Arctic of Canada.

2. This is one of the coldest regions of the Arctic. The epidemic occurred in the depth of an unusually severe winter.

3. It resulted in unprecedented devastation; in the Chesterfield area it killed over 5% of the total population and paralyzed 14%.

4. Spread appears to have been largely through the medium of clinically healthy carriers.

5. All ages except those under three were affected. No evidence of disease was found in children under three years of age and there were only two at the ages of three and four.

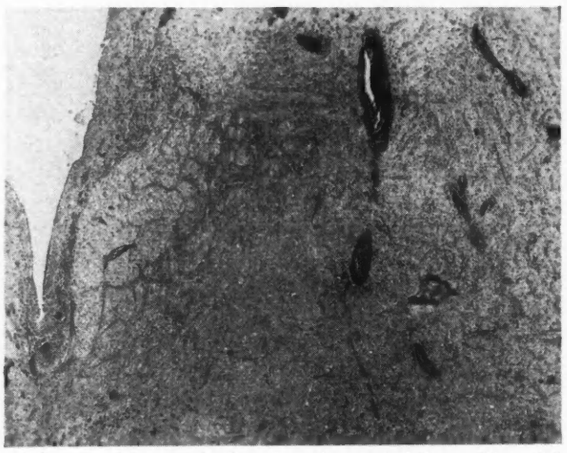

Fig. 7.—Floor of the fourth ventricle x 21. with the median fissure on the left. There is marked perivascular round cell infiltration. This infiltration was seen in sections of the basal ganglia. Sections of cortex were normal.

This suggests an absence of immunity except in the first few years.

6. The epidemic has been shown by monkey inoculation to be due to a poliomyelitis virus.

7. The brunt of disease from clinical signs and from pathological findings is shown to have fallen on the lower cord, whence it ascended to involve the respiratory muscles.

8. Very little evidence of meningeal, bulbar or cerebral involvement was found.

9. All the features of the epidemic suggest that in a non-immune community poliomyelitis behaves like any acute infectious fever.

REFERENCES

1. HOYGAARD, A.: *The Lancet*, January 28, 1939.
2. BERTELSON, A.: *Medd. Grnland*, 117: 75, 1935.
3. Poliomyelitis and Encephalitis, Manitoba, 1941. (A symposium arranged by the Department of Health and Public Welfare of the Province of Manitoba.)
4. DRAPER, G., DUPERTIUS, C. W. AND CAUGHEY, J. L.: Human Constitution in Clinical Medicine, p. 204.
5. DRAPER, G.: *Am. J. M. Sc.*, 184: 111, 1932.

PROBLEMS IN NEUROCHEMISTRY*

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BEFORE I begin my discussion proper I would like to philosophize briefly on the motivations or objectives which induce scientists to do their work, and the public to support it. This I do because it is necessary to understand my attitude in order to appreciate my subject.

Knowledge of the results and methods of scientific investigation is interesting. It gives a sound outlook on nature, and teaches discipline in thinking. A good experiment or a well based theory is a thing of beauty in itself. Therefore science has considerable cultural value. Close study of natural phenomena, by experiment or otherwise, is exciting and full of surprises. It titillates curiosity and desire for adventure. Application of the results of scientific investigation increases our power over nature in medicine, agriculture, industry and all aspects of human activity and behaviour. As a result science has great economic, social and, nowadays, political significance.

It is on the basis of the third aspect that scientific research receives most of its support. This, I think, is quite natural since the public is naturally interested in what it will get out of this activity and very little interested in merely letting scientists have a good time. The public is not particularly conscious of the cultural value of science. Many providers of research funds are nevertheless wise enough to realize that basic research is the root of the scientific tree and that unless it is nourished the tree will not bear much practical fruit.

Many scientists and others still consider, however, that the only valid motivation for basic research is pure personal curiosity. Any consideration of ultimate practical value is, by some, regarded as sullying the purity of their devotion to science and possibly contaminating the results of their work. This exaggerated outlook is not as common now as it used to be, and in any case it does little or no harm in many subjects and situations.

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* Presidential address, Montreal Physiological Society, April 25, 1949.

In my opinion frank applied research aimed directly at practical objectives should be regarded as work of equal status with basic research and not as a slightly venal activity. But such applied research, with all its ingenuity and need for thorough scientific understanding, is dependent on basic research.

With regard to basic research, I think we may consider three situations and types of men. There is the pure academic research worker who studies what interests him without reference to any practical problem. There is the scientist whose main work is definitely aimed at immediate practical goals but who may be held up for some basic information and has to find it out for himself. In between is the large group, to which I belong, whose field of interest, or financial support, is concerned with certain practical problems, but who feel that these cannot be solved without a great deal more basic but relevant research. We choose to, or have to, consider relevance to our ultimate objective. We may doubt whether we will actually solve the problems in our time, but at any point where our findings may be of practical value I believe we should feel it our duty to see that practical trial is made. To my mind the border between basic and applied research is vague and fluctuating and we should not hesitate to oscillate between the two. A life saved or a pain alleviated by application of principles we discover should be as much a reward for our work as the esteem of our academic colleagues. I have not so far used the word "pure research" because I do not believe there is such a thing. I think that all good research ultimately becomes basic to later work of practical significance.

In accordance with this philosophy, I consider that the objective of neurochemistry, the chemistry of brain and nerve, is the solution of problems concerned with injury and disease of the brain and nervous system and of the mind. Thus I tend to consider first, in a very general way, what problems the neurologist, neurosurgeon and psychiatrist are concerned with and then what types of knowledge we require in order ultimately to help solve these problems. Actually, as you might guess, one soon comes to the conclusion that virtually no kind of information is too theoretical to be useful but, since everything cannot be found out at once, we should perhaps give priority to securing information lack of which is obviously holding up applied research. One also attempts to study biochemical materials and processes not purely as matters of biochemical interest, but as aspects of the physiological function of the organs concerned and of the whole organism. Further, it should be noted that even if we were interested solely in the functioning of the normal organism, pathological conditions, like artificial experimental alterations in the organism, often provide very illuminating exaggerations or caricatures of normal processes.

According to my approach, then, I think that it is the business of neurochemistry to acquire information useful in the study of three main groups of problems, namely neurological and neuromuscular diseases, brain and nerve injury and the effects of neurosurgery, and psychiatric diseases. The biochemical bases for these studies would be divided roughly into several divisions. First, clarification of the chemical and physical-chemical composition of brain and nerve material and the processes required to maintain these materials in their proper relations. Second, the chemistry of function which aims to elucidate the chemical processes which underlie nervous activity. Part of this aspect, and not easily separable from it, would be the processes concerned with recovery from activity, and the production and application of energy. Thirdly, one must consider the integration of the nervous system with the rest of the organism. Under this heading would come studies in endocrinology, nutrition, blood chemistry, circulation, respiration, etc., both from the point of view of the effects of these on the nervous system and their control by the nervous system.

I will start with some observations on the materials of nervous tissue. As you know, the high lipoid content of nervous tissue is perhaps its outstanding material characteristic as compared with other tissues. The lipid nature of white matter and myelin sheath is obvious from its appearance. The first neurochemist, Thudichum, quite naturally chose the brain lipoids for his studies. He did truly remarkable work for the time, around 1865-1882, partially separating and characterizing a number of the complex lipoidal substances of brain and quantitatively determining some of these as well as sundry other substances. More complete separation and chemical characterization

of the lipoids has gradually been achieved by various workers, but only in the last couple of years has it been shown, by Folch, that cephalin consists of a mixture of three phospholipids, two containing the nitrogenous bases ethanolamine and serine, and one nitrogen-free inositol, an interesting substance from various points of view.

As yet we have practically no idea of the function of the lipoids in nervous tissue. It is believed that the myelin sheath serves as an electrical insulator but such a suggestion does not explain the need for such a variety of very complex chemical structures. Studies with isotopes indicate that the turnover of the phospholipids in the brain is quite slow, so that they may not take a very active part in the dynamics of nerve function. Clues to the rôle of the complex lipoids will probably be gathered by physical chemical studies of their properties and by observations on differences in behaviour between myelinated and non-myelinated nerve fibres, and on changes which are concomitant with the onset of myelinization. The ability of myelinated fibres to function seems to appear at the same time as myelinization occurs. Some years ago, Libet and I observed that the integrity of the lipid material of brain tissue seems necessary for its normal metabolism. A system consisting of an iron compound and ascorbic acid caused rapid oxidation of brain phospholipid followed by great inhibition of normal respiration.

The group of demyelinating diseases, particularly multiple sclerosis, constitutes one of the greatest problems of neurology and further knowledge of the nature and rôle of myelin is essential to its solution. Just recently a methodical quantitative study on the lipoid distribution in grey and white matter of adult and infant animals, and of peripheral nerve, by methods requiring only small samples of tissue has been undertaken by Johnson, McNabb and Rossiter at the University of Western Ontario. They conclude that the material of the myelin sheath consists mainly of cerebroside, free cholesterol, and sphingomyelin, rather than lecithin and "cephalin". Having obtained this information they are now able to show what changes occur during degeneration of the distal portion of severed nerves. It will be most interesting to know whether the same types of change, or different ones, occur during demyelinating diseases. I feel that some very interesting ideas will emerge as we discover the functional significance of lipid structure. Consider, for instance, the fact that choline is a constituent of lecithin and sphingomyelin and of acetylcholine, it has a vitamin-like activity in fat metabolism and is one of the molecules concerned in the process of transmethylation. Also, Corteggiani has evidence that acetylcholine is bound in brain tissue in some sort of phospholipid linkage.

The protein chemistry of nervous tissue is at last receiving attention. Folch has isolated two rather pure proteins from brain and it will be most interesting to know what, if any, enzyme activity is associated with them. Hydén and Hartelius, in Caspersson's Institute, find a high capacity for protein synthesis in the nerve cell body, particularly in the nucleus, which is intimately connected with the activity of ribose nucleic acid, and they find that hyperstimulation causes a marked loss of protein which is later restored. They find lowered protein and synthetic capacity in cells with vitality impaired by ischæmia or otherwise and in nerve cells from brains of certain psychotic patients. They have been investigating a substance, malononitrile, which seems to increase protein synthesis in nerve cells and which they think is of value in treatment of some mental diseases.

In muscle chemistry, now that the main picture of the mechanism of carbohydrate and fat combustion and the production of energy has been worked out, the structure and properties of the contractile protein complex, actomysin and its intimate association with adenosine triphosphatase activity provide the most exciting developments. I feel that work on the proteins of nervous tissue, their enzymic activities and their relations with the complex lipoids, is likely to bring us similar fascinating new ideas. It seems probable that the main activity of nerve, the transmission of impulses, is a function of its surface and already three very significant enzyme proteins, cholinesterase and adenosinetriphosphatase, and pyruvic dehydrogenase, have been found to be localized in the nerve sheath.

Our most detailed knowledge of the chemistry of nervous tissue concerns its energy metabolism and the metabolism of acetylcholine. Much of the ground work of both of these fields was laid down by Quastel, the second neurochemist. I cannot go into details of the vast amount of

work that has been done in these two fields but will just mention a few points that interest me.

The study of energy metabolism, by which I mean oxygen usage, the consumption of substrate, the splitting of carbohydrate to lactic acid, and the enzyme processes concerned, has been made chiefly on tissue *in vitro*. The correlation of these studies with recent studies on the living animal may lead to significant new developments. Schmidt and Kety, and Geiger and Magnes, have worked out new methods for measuring total cerebral circulation and metabolism *in vivo*. Davies has developed methods for studying local oxygen tension and consumption on the brain surface. Their results show that brain oxygen consumption varies widely with neuronal activity. As far as I can judge, the usual values for brain tissue oxygen consumption *in vitro* correspond roughly to the rates obtained *in vivo* in resting or depressed conditions. *In vitro,* the rate can be increased by high concentrations of potassium or by deprivation of calcium but, in our experience, the increase is not as great as is produced *in vivo* by a convulsion. The mechanism by which increased metabolic rates are released *in vivo* is something we would like to know.

Brain tissue has a high capacity for the formation of acid, lactic acid, from glucose. This occurs in the absence of oxygen and also at a considerable rate aerobically. Figures obtained on men by Gibbs *et al.* show that *in vivo* about 16% of the glucose utilized by the brain is converted to lactic acid. It has long been a feeling of mine that this glycolytic capacity of brain must have significance in the regulation of physiological function. Its effect could be exerted in two ways. The acid formed within the cell would be expected to alter conditions at the cell boundary, and the acid emerging into the brain fluids would affect the local blood circulation since cerebral vessels are very sensitive to pH charges.

The enzyme systems in brain tissue which are concerned in carbohydrate metabolism have been well studied and are not obviously different from those of other tissues. A number of studies, particularly by Stone and his coworkers, have been made relating carbohydrate enzymology to conditions *in vivo*. Anoxia, or trauma which produces local anoxia, and convulsive activity which produces an oxygen demand exceeding the supply, result in the accumulation of lactic acid and in decreases in high energy phosphate compounds, as might be expected from knowledge of the mechanisms of energy supply obtained *in vitro*.

Hoagland has made a very suggestive study combining ideas of enzymology with electrophysiology and thermodynamics. He observed the electroencephalogram (brain waves) of human subjects at different temperatures and, from analysis of change of frequency of the α rhythm with temperature, was able to calculate the energy of activation of the chemical reaction which limited the overall energy producing mechanism. In normal subjects the value of this energy of activation suggested that the succinate-succinic dehydrogenase system was the limiting reaction, but in advanced general paresis there was a shift which suggested that the cytochrome-cytochrome oxidase reaction had become the limiting reaction in the respiratory mechanism.

Under normal conditions brain tissue *in vitro* or *in vivo* consumes glucose almost exclusively. But when deprived of this substrate it can consume non-carbohydrate material. The nature of this material has not been demonstrated but it is probably partly protein or lipoid which is normally part of the tissue structure. I have suggested that the alteration produced by this consumption of structural material in the absence of glucose might be the basis of the effects of the insulin shock treatment of psychoses.

Brain tissue is able to oxidize only one of the amino acids, glutamic acid. This fact leads into a tangled mass of intriguing observations. Glutamic acid causes a marked increase in acetylcholine synthesis by certain brain tissue preparations. It undergoes the transamination reaction with oxaloacetic or pyruvic acid. It combines reversibly with ammonia to give glutamine. (Very recently Richter has shown marked changes in ammonia content of brain in relation to convulsions or narcosis.) Glutamic acid has been found by J. R. Stern to be absorbed and concentrated by brain tissue *in vitro,* and Krebs finds that it helps prevent loss of potassium from such tissue. It has been claimed that feeding glutamic acid benefits petit mal epileptics and increases the intelligence of children and the maze-learning ability of animals. (These claims have not all been satisfactorily substantiated.) Recently it

has been found that glutamic acid somehow brings out the flavour of some foods and it is now on the market in sauces and the like. Finally, glutamic acid is one of the most prevalent amino acids in proteins. A synthesis of all these and other related observations would probably be of great significance.

The situation with regard to acetylcholine is full of interest both from the scientific and the human points of view. It is the centre of intense controversy, in which the emotions of the protagonists become considerably involved. This is not, in my opinion, a bad situation as long as the judgment of the merits of the arguments remains in the hands of scientists and no external pressure to adopt a particular theory is applied. The acetylcholine story is the focus at the moment of the study of the chemical dynamics of nerve function. It is well to have the stimulus of controversy applied to this central problem of neurochemistry and neurophysiology.

Stated extremely briefly, the facts upon which most workers are agreed are as follows. Acetylcholine is an intensely powerful pharmacological agent producing effects like electrical or other stimulation. It can by synthesized by nervous tissue. A substance called "acetylcholine precursor" or "bound acetylcholine" exists in nervous tissue and releases the pharmacologically active substance very readily. Acetylcholine is released in various parts of the nervous system during activity, and nervous tissue contains an enzyme, cholinesterase, which hydrolyzes acetylcholine rather specifically. The theory of Dale and Loewi is limited to synapses and certain nerve-end organ junctions and states that the arrival of the impulse causes acetylcholine to be liberated at the nerve endings and this liberated chemical stimulates the next nerve cell or the end organ. This theory of chemical transmission has been disputed by those physiologists who believe in purely electrical transmission, but it seems probable that neither theory is complete and both represent aspects of the same truth. A unified theory has been put forward by Nachmansohn who believes that acetylcholine release initiates the electrical phenomena and the electrical changes are responsible for the synaptic transmission. But his theory goes further since he believes that his evidence indicates that the acetylcholine mechanism is responsible not merely for the crossing of synapses but for the propagation of the impulse along the nerve in all nerves and also in muscle. This pleasant, simplified theory is under hot attack.

There is no doubt in my mind that acetylcholine plays some important rôle in nerve function, though, in apparent reaction from Nachmansohn's theory of the comprehensive rôle of acetylcholine, some workers even doubt this much. But we still do not have any biochemical picture of how acetylcholine exerts its effects; we have no idea of the significance of its structure. The same applies to adrenaline or sympathin, the other main neurohumoral agents.

The rôle of metals, their ions and complexes, is a very significant problem in many fields of biochemistry and particularly in neurochemistry. The potassium ion seems to be a key factor. It seems to be the only ion other than hydrogen ion to which nerve and muscle cells are freely permeable under normal conditions and, as a result, it is concentrated inside these cells. The resting potential of nerve is often ascribed to a Donnan effect based on this selective permeability; and the old theory of the action potential, now rather shaky, was that a breakdown of this selective permeability occurs with passage of an impulse. Potassium is liberated on stimulation of nerves and application of potassium salt to synapses and neuromuscular junctions causes the post-synaptic cell to fire. There seems to be a definite relationship between potassium and acetylcholine. Both have stimulatory effects, though the latter is about a thousand times as active as potassium. Application of either to various nervous structures causes release of the other. *In vitro* Quastel and his co-workers showed that high potassium concentrations cause release of acetylcholine from the bound material in brain tissue and, probably as a result of a disturbed equilibrium, a greatly increased synthesis of acetylcholine. Potassium has since been shown to be essential in the purified enzyme system which synthesizes acetylcholine. There is some evidence that there is a base exchange reaction between acetylcholine and potassium and the protein complex which holds acetylcholine in the inactive, bound, form. Potassium is also concerned in certain of the enzyme reactions concerned in the breakdown of carbohydrate.

And finally, high concentrations of potassium stimulate the respiration and aerobic glycolysis by brain slices. These facts clearly suggest that potassium movements are concerned in functional activity and in regulating the supply of energy for this activity.

Calcium is almost as interesting as potassium though its actions are more or less the reverse of those of potassium. Bronk and others have shown that the excitability of a nerve is increased as the calcium ion available is decreased. If citrate, which forms an unionized complex with calcium, is added to the medium to reduce the available calcium ion to a minimum, the nerve commences to fire rhythmically, spontaneously. A couple of Russian authors have reported that diffusible calcium in brain is increased by 60 to 70% under ether narcosis. Brain tissue respires more actively in the absence of calcium than in its presence though the rate falls off sooner. The calcium ion seems to have a stabilizing influence on both nervous and energy-producing activities. Calcium is also concerned in adenosine triphosphatase activity.

Magnesium, which is known to play an important rôle in the metabolism of pyruvate and hence of carbohydrate, is, of course, essential to nervous as well as other tissues but it also has anæsthetic properties which make it specially interesting to neurochemistry. The commonest ion of all, that of sodium, has recently been found to be a strong inhibitor of glycolysis in extracts from brain. Sodium is not normally present in high concentration in intracellular fluids but presumably it could enter nerve cells and exert an effect under conditions of increased permeability.

It seems to me that the most interesting developments in the chemistry of nerve function will occur when a theory is advanced which satisfactorily draws together knowledge of the interrelations of acetylcholine, potassium, calcium and other factors.

In order to understand the mechanism of nervous and mental diseases and the effects of trauma we need to know the mechanisms by which many factors affect nervous activity. Quastel showed that narcotic drugs depress the respiration of brain tissue *in vitro*. We now know fairly precisely at what point in the chain of oxidation reactions this inhibition may occur. Small but definite inhibitory effects are noticeable at concentrations likely to exist in the fluids of a narcotized animal. But there is no proof that these inhibitions are responsible for the narcotic effects. Metrazol a convulsant drug, has a similar small inhibitory effect. The delta isomer of benzene hexachloride, which has a narcotic effect, strongly stimulates brain tissue respiration. However, some observations fit in with Quastel's findings. Westfall for instance, found that conditions which stimulate pyruvate oxidation, such as intravenous injection of pyruvate, shorten and lighten the effect of nembutal on rabbits.

With regard to convulsant drugs we are almost totally in the dark. Only in the case of drugs which are known to inhibit cholinesterase have we any inkling of how convulsants work. Even with the simplest chemical convulsant, oxygen at high pressure, the situation is baffling. High oxygen tension will gradually depress tissue respiration *in vitro*. It causes inhibition of many enzyme systems, apparently chiefly by oxidizing essential sulfhydryl groups in the enzyme molecules. Further, the systems concerned in glucose metabolism upon which brain is especially dependent, are specially susceptible. But the convulsive and lethal effects of high oxygen tension are much more rapid than can be accounted for by known enzyme inhibitions and tissue removed from an animal killed by high oxygen tension behaves normally. Just recently a report has appeared which states that very low concentrations of a number of convulsant agents inhibit carbonic anhydrase while anticonvulsant agents stimulate it. I think this will need confirmation before we theorize about it.

It must be remembered that practically any neurotropic drug has both excitant and depressant effects, depending on the dosage and other factors, and this will have to be considered in the chemical analysis of their effects.

Explanation of the action of convulsant and anticonvulsant drugs is particularly relevant to the study of epilepsy. It should be borne in mind that convulsions occur as a result of a very wide variety of conditions. Epileptic convulsions may be due to the presence and action of some abnormal chemical agent with properties like those of known chemical convulsants. The presence of such an agent, guanidine, in the blood of essential epileptic patients has

been reported but we have not been able to confirm this. Epilepsy may result from derangement of neuronal metabolism, possibly some change in the acetylcholine mechanism causing a lowered threshold to stimulation. There is some evidence that acetylcholine metabolism is altered but no evidence that this change is primary to the condition. No evidence that the mechanisms of energy metabolism are altered could be found. My own feeling is that the neurones are fairly normal but that abnormal local conditions, possibly circulatory derangements, provoke abnormal behaviour. It is known that, at least in tissue extracts, glucose can inhibit acetylcholine synthesis; synthesis at low glucose concentrations is more rapid than at the normal blood level. I have already referred to the possible effects of lactic acid production. Both glucose concentration and glycolysis would be affected by circulatory changes. I believe, therefore, that more needs to be known concerning the inter-relation of energy metabolism, that is, oxygen and glucose utilization and glycolysis, and acetylcholine metabolism or other chemical aspects of function. The mechanism of the effect of the ketogenic diet in the control of epilepsy is, I believe, completely unexplained but should provide a clue to the chemistry of epilepsy. Of course it is possible that neurophysiologists may be able to explain epileptic hyperactivity purely in terms of derangement of the complex neuronal circuits, but this would not exclude the possibility of control of the hyperactivity by chemical means.

The neuromuscular diseases raise some most interesting problems and at the same time offer important clues to the understanding of chemistry in relation to function. In periodic paralysis there is a clear relation to potassium metabolism. The usefulness of prostigmine and the effects of DFP, both cholinesterase inhibitors, in myasthenia gravis, are strong evidence for the rôle of acetylcholine in neuromuscular transmission and indicate the type of chemical defect in this disease. Certain staining reactions indicate specific changes in the muscle protein in other neuromuscular diseases. Such observations, if followed up by biochemical and biophysical techniques, might throw light both on the nature of the disease and on the chemistry of normal function.

Though intracranial and intraspinal tumours provide some of the commonest and most serious problems of neurology, the basic study of these new growths perhaps belongs in the field of cancer research. However, it is likely that application of classical methods for the study of tissue metabolism might be a help in the classification of such tumours and in estimation of malignancy and of value to general cancer research.

I do not intend to do more than mention one or two of the fields of neurochemistry involving the relation of the nervous system to other parts of the body. Much information may in the future be obtained from blood studies carefully interpreted. Elevated blood and spinal fluid pyruvate has been reported in various neurological conditions, indicating decreased thiamine activity; the uric acid level is said to be raised following diathermic stimulation or lesions of the sella turcica region. Since Claude Bernard's observation of the effect of puncture of the floor of the fourth ventricle it has been known that blood sugar is affected by factors affecting parts of the brain; conversely the effect of lowered blood sugar on brain function is well known. Toxic substances such as various amines, formed in the intestine and elsewhere, can affect mental and nervous processes. Neuroendocrinology could be a whole field in itself. Endocrine organs are under partial control of the nervous system and, conversely, the function of nervous tissue is probably to some extent affected directly by endocrine factors, and certainly indirectly.

I think the development of physical chemical aspects of neurological science needs special attention. Many of us feel that nervous function is a surface effect depending upon varying orientation of complex molecules and permeability to ions. Until we have more knowledge and a clearer synthesis of known facts in this field, we will be in the dark with regard to the basic mechanisms of nervous function and dysfunction.

The composition of the cerebrospinal fluid has been well studied, and some properties of the barriers which separate this fluid from the blood, and the brain from the blood, have been worked out. Elementary consideration of this knowledge and of the buffer mechanisms of physio-

logical fluids has led to some interesting observations on cerebral blood vessel reactions and brain pH, and to the use of a solution which seems useful in some neurosurgical cases where large intracranial spaces have to be filled. But we should know more about the composition of the interstitial fluids of nervous tissue and about factors which affect cerebral blood vessels. This sort of knowledge is necessary for the understanding of the very practical problem of cerebral œdema, which occurs following trauma and in various other conditions, and often complicates neurosurgery. Solution of this problem also depends upon information concerning the type of chemical changes which nervous tissue undergoes following disruption of neurones and supporting cells and of circulation.

Finally, we should mention what is probably the greatest group of problems to which neurochemistry might contribute, namely the mental diseases. A very great deal of work has been done on the blood chemistry in neuroses and psychoses but the only real conclusion reached is that there is greater variability in nearly all blood constituents in mental disease than in normal, and often there is disturbed sugar tolerance. There seems to be a failure to respond to circumstances, a defect of homeostasis, and this conclusion is passed on to the endocrinologists for investigation. There are a few mental deficiencies and disturbances in which clear biochemical abnormalities are evident. One might mention the dementia of niacin deficiency, the mental defect accompanying an inborn error of metabolism, phenylketonæmia, and the alcoholic and other toxic psychoses. It might be mentioned that Quastel found evidence of a faulty detoxification mechanism in some patients diagnosed as schizophrenic. Study of these and other rather tangible conditions should give us some useful leads concerning factors which affect the mentality and emotions.

There is a general tendency among workers in the field to relate mental symptoms to abnormalities in energy production as a result of anoxia, lack of substrate, or interference with the relevant enzyme systems. Danziger lists 52 compounds and 9 elements which produce symptoms of mental disorder, and he attempts to relate their effects to the production of tissue "anoxia". Loevenhart long ago found that breathing carbon dioxide had striking, temporary, beneficial effects in some psychotic patients. I think this result might be due to an effect of carbon dioxide in improving cerebral circulation. There are sundry other clues to the chemistry of mental disease. The insulin shock treatment is presumably a biochemical interference with brain metabolism and further study should indicate the mechanism of its effect. Similarly, the electric shock treatment must have chemical effects. Possibly the observation of Hydén and Hartelius, mentioned earlier, on protein synthesis and the effect of malononitrile may come to something.

Ashby suggests that quantitative determinations of the activities and distribution of enzymes in the brain might throw light on the nature of mental derangement. She suggests that enzymes chosen for study should preferably be ones which are known to be inhibited by substances which cause mental symptoms, and which seem to be limiting factors in function as judged by the relation of the time of their appearance to the onset of function in various regions, and which are stable enough to study in human autopsy material. She has chosen the enzyme carbonic anhydrase for study, and finds that it satisfies these criteria. She chose it initially because it is inhibited by sulfanilamide which can cause mental symptoms. It is a stable enzyme and she has shown that there is a close relationship between its appearance in the various parts of the brain and the onset of function. She believes there are deviations from the normal distribution in mental dysfunction. However, at present we do not know anything significant about the rôle of carbonic anhydrase in the brain except for the report on the way it is affected by convulsants and anticonvulsants. Ashby's studies must at present be regarded only as a model of a type of approach which may be applied to enzymes of known significance. Analogous studies would, of course, be applicable to all types of nervous disease.

Though we have very little real chemical insight into mental disease, I think such will be developed in time. However, I am not prepared to claim that the problem of mental disease is to be understood and solved only at the chemical level. Just as the biochemistry of a congenitally deformed foot or the stump of an amputated leg may be normal though the organ cannot perform in a normal manner, so an abnormal organization of neuronal connec-

tions, congenital or acquired, could result in unusual behaviour with a normal chemical basis. I am willing to admit that much mental disease may be psychogenic. But just as psychosomatic symptoms can be helped by the chemical tools of medicine and the underlying emotional disturbances may be approached psychiatrically with the aid of chemical tools such as the barbiturates, so also may purely mental conditions be helped by the chemical approach. Immediate symptoms of hypo- or hyper-activity may be chemically controlled while psychiatric reintegration may be aided by other chemical tools.

Though I have touched on many aspects of neurochemistry, I have not really attempted a comprehensive review and some of you may wonder why I have omitted many important points as well as much detail. But I believe I have indicated that the territory is wide and should be fertile. The ground will have to be cleared, stump by stump, and it may take a long time before a large harvest can be gathered. But a valuable yield should be obtained from many small plots as they are cleared.

AN EPIDEMIC OF PUERPERAL MASTITIS*

(Associated with Nasopharyngeal and Skin Infection in the Newborn)

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THE purpose of this paper is that of a preliminary report dealing with some aspects of an epidemic of puerperal mastitis, breast abscesses, and skin pustules in the newborn which has prevailed in Winnipeg for over one and a half years, and in particular the steps taken to control the epidemic amongst patients delivered in the Obstetrical Department of the Winnipeg General Hospital. Separate and much more detailed papers are under preparation by those concerned with the tremendous amount of laboratory work which has been undertaken during the investigation of the epidemic.

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HISTORY OF OUTBREAK

In order to give some idea of the problem that has confronted obstetricians in Winnipeg during the epidemic it is necessary to review very briefly the history of the outbreak, and to do this the four major Winnipeg hospitals concerned will be designated here as A, B, C and D—D being the Winnipeg General Hospital.

A special meeting of the Obstetrical and Gynæcological Section of the Winnipeg Medical Society was called to discuss the problem on August 26, 1948. The following were the main points brought out at that meeting:

1. The epidemic appeared to commence in December, 1947 in Hospital A and very soon was affecting patients delivered in Hospitals B and C.

2. The common course of the infection was that the newborn infant developed angry-looking pustules within a few days or weeks of delivery; these responded to a variety of local treatments if adequately applied. The parturient woman developed a mastitis which rapidly became an abscess on an average of six weeks after delivery, but the time range was from two to twelve weeks.

3. It had soon been found that the responsible organism was resistant to the sulfa drugs and to penicillin in very large doses; in fact, no method had been found to prevent abscess formation once mastitis was established in most cases. Abscesses invariably required surgical drainage.

4. *Staphylococcus aureus hæmolyticus,* coagulase positive, was isolated from practically all cases of pustules in infants and puerperal breast abscesses.

5. The organisms appeared to have a special affinity for maternal breast tissue and infants' skin, since there had not been any increase in other septic lesions in the obstetrical departments concerned.

6. Each of the affected hospitals had in turn taken the standard measures to eliminate the infection from their wards: they were closed for thorough disinfection, repainting of the nurseries, reduction of overcrowding where possible, and new rules for visitors and ward technique were drawn up and put into effect.

In each case, after a short respite, pustules once again began to appear on infants in the nurseries, shortly followed by cases of mastitis and breast abscesses among the mothers. August, 1948, was reported to be a particularly bad month in the hospitals affected.

7. Representatives from Hospitals A, B and C all expressed amazement that D had been completely free of the epidemic up to that time, since some of them gave estimates of over 15% of all women delivered as the incidence of breast abscess.

The meeting ended with the appointment of a committee to investigate the problem and in due course make recommendations for the control of the epidemic. This committee consisted of a representative from each of the four hospitals, Dr. Maxwell Bowman of the Department of Health and Public Welfare of the Province of Manitoba, Dr. J. C. Colbeck, Director of the Manitoba Provincial Laboratory and a pædiatrician from Hospital A.

This committee held six meetings from September 2, 1948 to May 31, 1949 inclusive. It was soon evident that the problem was most likely to be solved in the laboratory and to that end Dr. Colbeck deserves great credit for the work he did outside his regular duties. At the second meeting of the committee, held September 28, 1949, he was able to report that he had obtained the necessary materials and had already carried out phage typing of the organisms obtained from many samples of pus from both breast abscesses and infant pustules, and that he was already convinced that one particular phage type of the *Staph. aureus* was responsible for the outbreak. He named this the "Winnipeg strain" or "phage W strain". He had also found that nose and throat swabs taken from all the staff of the Obstetrical Department of Hospital A showed that 60% were positive for *Staph. aureus hæmolyticus* and that a few of these proved to be of his phage W strain. He suggested that all the staff concerned at Hospital A should have their noses sprayed three times daily with penicillin solution (1,000 units per c.c. of normal saline); this was carried out for just over a month and proved to reduce the carrier rate but not to eliminate them all.

The committee caused an impartial survey of the Obstetrical Departments of Hospitals A, B, C and D to be carried out in November, 1948, with a view to comparing the physical layouts, ward techniques and rules, and any possible differences which might account for the varying incidence in the epidemic. This survey was carried out in minute detail but no useful conclusions could be drawn from it; the only obvious conclusion was that from the physical layout alone Hospital D *should* have been the most seriously affected, whereas at that time there had been no cases of either serious pustules in infants or puerperal breast abscesses.

The use of an autogenous vaccine was suggested but correspondence with the Government Laboratory, Ottawa, and the Connaught Laboratory, Toronto, suggested that such a vaccine was not likely to be of any value.

By February, 1949, it was found that the incidence of both infant pustules and puerperal breast abscesses had fallen considerably in Hospitals A, B and C, but cases continued to occur in all three. Dr. Colbeck at that time reported that pus from the first 100 breast abscesses that he had examined proved to be *Staph. aureus* in all cases and that 89% were his phage W strain.* He also reported details of an experiment carried out in Hospital A:

1. Swabs from nose and throat of 120 babies in the nurseries showed 64 to be carriers of *Staph. aureus* and that 32 were his phage W strain, that is, 26.7% of the babies swabbed were carriers of the virulent strain of staphylococci.
2. Swabs from the nose and throat of some 70 mothers on admission to the Obstetrical Wards showed that 22% carried *Staph. aureus*, but that only 2 of these were of the phage W strain.
3. Swabs taken from 68 mothers at the time of discharge from the obstetrical wards showed 23.5% to carry *Staph. aureus* but only one was the phage W strain, and it was noted that the *Staph. aureus* carriers on discharge were not always the same ones who had the organism on admission.

This would seem to indicate that the reservoir of infection for the phage W strain was in the hospital and that the babies were exposed to it.

Dr. Colbeck carried out swabbings in Hospital D in March, 1949, with a view to using his findings as a control since at that time the epidemic had not manifested itself there. The results, however, only served notice that this hospital was about to experience the outbreak in the very near future for it was found that of 53 babies swabbed in the nurseries 16 proved to carry the phage W strain of *Staph. aureus* (30.2%). Thus it was obvious that although we had not experienced the epidemic the causative organism was already well established in our nurseries. At that time all the staff con-

* A more recent review has shown 95% are phage W strain.

nected with the obstetrical department of this hospital (D) were swabbed (nose and throat) and only one was found to be positive for the phage W organisms, but it is perhaps significant that he was a staff pædiatrician who was frequently in the nurseries.

EVENTS IN THE WINNIPEG GENERAL HOSPITAL

At the outset it must be stated that we consider ourselves to have been very fortunate to have escaped the epidemic in this institution for so long, and further, when the infection did occur here we were able to benefit from the experience in the other hospitals and in particular from all the work done by Dr. Colbeck and the special committee mentioned above.

The records of this hospital show the following incidence for breast abscesses drained during the years 1945-47:

1945 — 2 (one not puerperal), 0.07% of 1,436 deliveries.
1946 — 7 (two not puerperal), 0.23% of 1,728 deliveries.
1947 — 4 (one recurrence in the same woman), 0.19% of 2,030 deliveries.

NOTE.—The records do not show where any of these women were confined.

During 1948 there were 1,844 deliveries in our Obstetrical Department and of these four developed breast abscesses that had to be drained, an incidence of 0.216%. In addition, 18 other breast abscesses were drained in our theatres among women delivered elsewhere.

As was mentioned previously, Dr. Colbeck showed in March that a reservoir of *Staph. aureus* of the phage W strain was definitely established in our nurseries, since 30% of the babies' nose and throat swabs were positive. It was not until early in April, however, that clinical manifestations of the infection began to occur, as evidenced by the sudden increase in the number of pustules developing in babies before they left hospital. Petrie dishes with culture medium were then exposed to the air in various parts of the obstetrical department, and on April 19 it was reported that a plate which had been exposed in one of the case rooms had produced a growth of *Staph. aureus* of the phage W strain. The superintendent of the hospital was at once informed and the decision taken to close that case room at once and admit no further cases to the ward which it served; as patients were discharged the whole ward was scrubbed down, the nursery and case room repainted and all utensils on the ward disinfected. That ward was completely closed from April 27 to May 2, 1949. The remainder of the department was then closed in sections for the same treatment.

As chief of the department I (F.G.McG.) convened a meeting of the obstetrical staff of the hospital to which were invited the superintendent, the matron and nurse in charge of the department, Dr. Colbeck, the Professor of Pathology and several of his staff, the pædiatric staff, a representative of the Skin Department and Dr. Bowman, secretary of the special committee referred to above. After a lengthy discussion a new set of rules for the Department were drawn up and agreed upon, to be put into effect as soon as the wards were reopened (see Appendix I). An "aureomycin committee" was also appointed at that time, whose chief function was to determine when and how much of the antibiotic should be used. (It should be mentioned that individual obstetricians and pædiatricians had been reporting excellent results in the treatment of the infant pustules by oral administration of aureomycin to the infant.)

The new regulations for the obstetrical department were put into effect May 10, the day it was again fully opened. At the same time the aureomycin committee undertook a con-

TABLE I.

1949 STATISTICS

Month	*Deliveries*	*Abscesses**		*Pustules*		
		No.	*Percentage*	*No.*	*Percentage*	
January plus February	326	5	1.05	0	0	
March	184	9	4.9	4	2.0	all phage W strain
April	143	13	9.1	29	20.2	
May	185	11	5.9	20†	10.8	
June	165	0‡	0	5	3.03§	

* Shown under the month of delivery, *not* the month when opened.
† All but one of these occurred before May 27, when aureomycin was administered to all newborn.
‡ It is too soon to be sure that some cases will not develop.
§ These were all doubtful lesions and on swabbing *none* proved to be staphylococcal.

trolled experiment on one of the wards: every other newborn was given a course of aureomycin by mouth consisting of three or four 25 mgm. doses (depending on the infant's weight) daily for five days .

Nose and throat swabs have been taken repeatedly from all staff connected with the obstetrical department (including the attending physicians) and it is of interest to note that most of those who have been found to be carriers of the phage W strain of *Staph. aureus* have been on nursery duties. In addition to the pædiatrician previously mentioned one obstetrician has been proved to be a carrier. All carriers have been given a course of aureomycin by mouth (250 mgm. four times daily for 8 or 10 doses) and then were found to be clear of the phage W organism, with one exception, who required a repeat course of the antibiotic. Carriers among any of the ward staff were taken off duty until negative swabs were obtained, with the exceptioon of a few key personnel who could not be replaced owing to the acute shortage of staff throughout the hospital.

It was very soon apparent that closing and cleansing the wards was not the answer to the problem, as pustules began to appear on babies within a few days of the reopening, and it was not long before the isolation unit which had been set up (for four mothers and their infants) could not cope with the cases occurring. Finally, on the morning of May 27 four fresh cases of pustules were reported and the aureomycin committee at once decided that *all* infants would from then on be given the aureomycin course outlined above, even though this did destroy the value of the controlled experiment which had been started on one ward. This decision was reached because not one infant who had been given aureomycin as part of the above mentioned controlled experiment had developed pustules.

To date* the administration of aureomycin to the infant seems to have proved to be the only certain method of controlling the outbreak, for no baby has developed a serious pustular infection who has had the aureomycin course, and *not one mother* whose newborn infant had the course has developed a breast abscess.

* July 20, 1949.

SOME CLINICAL OBSERVATIONS*

By February of this year Dr. Colbeck had shown conclusively that a high proportion of the infants in nurseries showed positive throat and nose cultures for the phage W strain of *Staph. aureus,* whereas the sampling of the population as a whole as judged by the pregnant women admitted to the maternity wards indicated that this virulent organism was not widespread outside the hospitals. This latter sampling has been repeated in the Winnipeg General Hospital commencing May 10, 1949, from which date nose and throat swabs were taken from every woman admitted to the obstetrical department, and whenever possible the husband or other visitor was also swabbed at the time of his first visit. Of the first 330 swabs from patients and 100 swabs from husbands, only one of each category proved to be a carrier of the virulent phage W strain of organism, and they were a husband and wife. It is interesting that the infant of this couple, born May 29, who was given the by then routine aureomycin course has not developed pustules and the mother has had no breast infection.

We have had a considerable experience in the use of aureomycin to prevent breast abscess formation among puerperal women once signs of mastitis have appeared. One of us (G.S.M.) had remarkable success with the first case in which the antibiotic was tried for this purpose.

The patient (an intelligent ex-nurse) was delivered March 22 and reported mastitis developing March 31, with a temperature just over 100° F. She was started at once on sulfathiazole and fomentations and told to report 24 hours later if there was no improvement. April 1 she reported that her temperature was 102.4° and that the pain and redness of the breast had increased considerably. She was visited at home and there was no doubt but that all conditions were present for the early formation of an abscess. It was decided to try her on a course of aureomycin for two reasons, (1) expense was not a vital consideration in her case (the local price was $21.50 for 16 250 mgm. capsules) and (2) one of us (G.S.M.) had recently heard of the excellent results obtained in the treatment of phage W staphylococcal furunculosis in infants by a pædiatrician from Hospital A. She was ordered to take one 250 mgm. capsule by mouth every three hours for 16 doses; within 24 hours her temperature was normal and most of the pain gone from the breast and within 72 hours there was no evidence of the former angry lesion. On April 6 the same patient reported that another abscess was beginning to form, this time in the same breast but in a diametrically opposite lobe. She was again given the same aureomycin course with even more rapid resolution. On April 27 she reported that she had developed a mastitis in the opposite breast and once again aureomycin caused rapid resolution.

* Cases quoted are from the authors' private practice.

In the light of subsequent experience the obvious mistake made in the handling of this case was that she was not over-ruled in her desire to continue nursing the infant until the third threatened abscess had occurred; obviously the infant was re-infecting her breasts each time she was cleared up with aureomycin. This case would also seem to afford clinical evidence that very little of the antibiotic could have been secreted in the breast milk since the child must have retained the infection in its mouth. It is also of interest that the infant in this case did *not* at any time develop skin pustules.

Subsequent experience with cases of puerperal mastitis treated with aureomycin in the same dosage as mentioned above proved that unless the antibiotic was given within 48 hours of the onset of the first signs and symptoms of breast inflammation, abscess formation was *not* prevented in most cases, but it was noted that when "aureomycin failures" were subjected to surgical drainage there was an astonishingly rapid recovery on the part of the patient and further, that they did not show the usual reaction which follows the opening of a multiloculated breast abscess.

It became our invariable rule that once the infant developed a serious pustular lesion it was taken off the breast at once; the infant was given a course of aureomycin and the mother a prophylactic injection of 300,000 units of (Tubex) penicillin. (Laboratory experiments have shown that the phage W organism will grow readily on a culture medium to which is added the equivalent of a large dose of penicillin. However, a normal dose of penicillin seems to clear a minimal breast infection, since a few cases of very early mastitis in which the milk proved to grow the phage W *Staph. aureus* were "cured" by penicillin, and mothers of babies developing pustules who were immediately given penicillin and at the same time ordered not to nurse the infant have not developed breast abscesses in some instances.) Aureomycin was not administered routinely to the mothers in early cases because of the expense involved.

In our experience the "flushed" or "caked" breast is most susceptible to infection, and once infection has occurred in such a breast neither penicillin nor aureomycin will prevent the eventual necessity for surgical incision and drainage, but the latter antibiotic will delay the formation of the frank abscess, so much so that in a few cases pus was eventually evacuated from a breast which had at no time been especially tender or reddened and the patient's temperature had never risen above 100°. One of our patients was delivered March 3, 1949, and developed a "caked breast" April 1; she was given stilbœstrol 5 mgm. t.i.d. for 3 days at that time to reduce the congestion and also instructed to apply fomentations. This treatment had little effect so she was told to wean the baby and was given a further five day course of stilbœstrol, which dried up the breasts but did not reduce the large wedge-shaped area of caking in the right breast. The hard area remained moderately tender and very slowly became smaller in size, but eventually fluctuant softening occurred and a cold abscess was drained May 24; phage W organisms were grown from the pus.

One further case is of interest to indicate the hardiness of the phage W organism.

Mrs. T. was delivered May 4, 1949. May 24 she reported that the infant had developed a few pustules on its abdomen. She was visited at home, a swab taken from the mother's milk and from the infant's pustules (which did not appear typical of the present epidemic), the infant weaned and ordered an aureomycin course; the mother was given 300,000 units of Tubex penicillin. *Staph. albus* was grown from the infant pustule swab and no staphylococci were grown from the mother's milk. June 7 she reported that the infant had broken out in another crop of pustules, which on inspection proved to be much more angry looking than those it previously had. There was no evidence of breast infection of the mother at the time and since she was not nursing the infant she was warned of the possibility of infecting herself from the baby but was not given any medication. The infant was given another course of aureomycin and swabs proved to be the dread phage W organism. An enquiry was made to try to determine how the infant had become infected with the virulent organism and it was found that the parents had borrowed a crib from a friend who had been delivered in Hospital C in September, 1948, whose infant developed pustules about 10 days after birth and she herself had three consecutive breast abscesses opened at about weekly intervals in October, 1948. The crib had not been used by that family for two months before our patient borrowed it. (On June 19 the mother reported that she had had a sore breast for several days; she was given a course of aureomycin but an abscess had to be drained June 24; the pus grew phage W organisms.)

CONCLUSIONS

1. A brief historical survey of an epidemic of puerperal breast infections associated with nasopharyngeal and skin infection in the newborn which has been present in Winnipeg hospitals since December, 1947, is presented.

2. Original work carried out by Dr. J. C. Colbeck, Director of the Manitoba Provincial

Laboratory is briefly mentioned, particularly the significance of his findings as related to combating the epidemic.

3. The incidence of breast abscesses in the Winnipeg General Hospital since 1945 is reviewed and the incidence of pustular eruptions in the nurseries of that hospital during 1949 is presented.

4. Steps taken to combat the epidemic in the Winnipeg General Hospital are reviewed.

5. The conclusion reached has been that the best method of preventing the occurrence of puerperal mastitis and breast abscess is to ensure that the infant does not harbour pathogenic organisms in its nose and throat. This has been achieved by the routine administration of aureomycin to every newborn infant.

6. The absence of skin pustules on the infant does *not* guarantee that it is not infective to the mother; many infants who are heavy nasopharyngeal carriers of pathogenic organisms (the phage W *Staph. aureus* in the present epidemic) do *not* develop any pustular lesions.

7. Obviously the routine administration of aureomycin to all newborn is not justified except in the presence of an epidemic such as has been described and where it has been proved that the infant is the carrier.

8. Routine nose and throat swabbing of all staff connected with an obstetrical department will always show a very high incidence of carriers of *Staph. aureus hæmolyticus,* coagulase positive, but there is no means of determining whether these organisms are virulent until there is a clinical outbreak of infections. In the absence of an epidemic of infection phage typing of the organisms will serve no useful purpose; conversely, phage typing of the organisms during an epidemic will enable the bacteriological laboratory to identify carriers of the virulent strain of the moment.

APPENDIX I

CHANGES IN THE ROUTINE OF THE WINNIPEG GENERAL HOSPITAL OBSTETRICAL AND NEWBORN SERVICE

Prevention of Entrance of Infection into Wards:

A: 1. All patients to be swabbed on admission—night admissions by 8.00 a.m.; day admissions by 3.30 p.m. Husbands of patients to be swabbed on the occasion of the first visit to the ward.

2. The husband is the *only* one allowed to visit. A substitute may be named (one person only). Substitute visitor to be swabbed on first visit to ward.

3. All staff (doctors, nurses and ancillary staff) and visitors to be masked.

B: 1. Obstetricians (honorary attending staff and courtesy staff) will refrain from opening or otherwise treating breast abscesses.

2. Nose and throat swabs to be taken on all personnel: (*a*) when first assigned to the Department, (*b*) in the presence of intercurrent infection, and, (*c*) routinely every two weeks.

Prevention of Infection Within the Ward:

1. All babies with skin infection to be excluded from nursery.

2. Minimal handling of the babies with neither washing or inunction after delivery except for demonstration on day of discharge from Hospital.

3. Nursery nursing staff *only* to be admitted to the nursery. The nursery is *"out of bounds"* to all others.

4. Examination of babies to be done on the mother's bed or on a table provided, the examining doctor will wear cap, gown and mask and will wash hands beforehand.

5. All information on babies to be posted outside the nursery.

6. The study of the effect of aureomycin in prevention of infection of the newborn will be made.

Care of the Breasts: modification of the present care by—

1. Substitution of soap and water for boracic solution.
2. Addition of more lanolin to the wax papers.
3. Giving the patient separate balls of sterile absorbent cotton with which to bathe the nipples.

THE ORAL ADMINISTRATION OF UNDECYLENIC ACID IN THE TREATMENT OF PSORIASIS*

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THE etiology of psoriasis continues to be a mystery. Available facts gleaned from statistics are at variance according to the various authors. Psoriasis is said to have a familial tendency of 6%, in one series, ranging up to 25% in another survey. The incidence of the disease in males is noted to be about the same as in females. This chronic dermatosis comprises 3 to 6% of all skin diseases. The average age of onset is 20 years. On examining 5,527 children, Conelli[1] reported 96 cases (7%) with the youngest patient being 3 months. The disease is noted to be rare in coloured races and of infrequent occurrence in dry warm climates. Most psoriatics are improved by sunlight, but Lane and Crawford[2] reported 10% aggravated by exposure to sun.

The research bearing on the etiological factors has proved a baffling and unproductive problem to many investigators over the years. Etiological has been investigated in six main channels: (1) Parasitic and bacterial infection.

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(2) Disturbances of metabolism. (3) Neurogenic disorders. (4) Influence of rheumatic diseases. (5) Dysfunction of endocrine glands. (6) Vitamin deficiencies.

During the past ten years, much of the work published has been on fat metabolism. Interest in this particular approach was stimulated by Gruetz and Buerger,[3] who showed that their patients with psoriasis had excessive amounts of cholesterol, lecithin and phosphatides in their blood. They obtained good results by using fat-free diets.

Gates and his associates[4] pointed out that: (1) Patients with psoriasis are usually well-nourished. (2) The incidence of psoriasis in Germany decreased during the first Great War, when the fat content of the diet was low, and, (3) That the scales of psoriatics have an abnormally high fat content. In this study they found the blood cholesterol normal or below normal in 30% of cases, whereas in 70% it was above normal or at the upper limits of normal. Treatment with diets low in fat proved sufficiently interesting to warrant further study.

Rosen, Rosenfeld and Kosnow,[5] on the other hand, found their patients with psoriasis had hypocholesteræmia, using the cholesterol tolerance test described by Gruetz and Buerger. Hering,[6] in 1938, reproduced some of the above work and concluded that no relationship existed between psoriasis and disturbed fat metabolism. Madden,[7] in 1939, while he could not show hypercholesteræmia or disturbed tolerance to fat in his patients concluded that fat-free diets were of definite value in the treatment of some cases.

Considerable interest was aroused in 1936 by Dragstedt, Prolaska and Hermis,[8] who reported a "fat-metabolizing hormone" (lipocaic), derived from the pancreas. Administration of lipocaic caused an increase in blood lipids and a diminution of fat in the liver. Subsequently, Stewart, Clark, Dragstedt and Becker[9] reported some success in treating a few cases of psoriasis with this substance. Other investigators, however, have not confirmed these early hopes, nor have we been impressed with the results obtained in the use of this agent. During recent years, work has continued on lipocaic as well as on lecithin, pancreatic extracts and sarsaparilla, etc.

Fat metabolism, then has been the central point of investigative effort in most of the recent research in the endeavour to discover the etiological factors of psoriasis. The internal use of the unsaturated and saturated fatty acids, as dermatologic therapeutic agents, was first suggested by Perlman.[10] He employed undecylenic acid in the treatment of a series of cases of tinea capitis, hoping by this procedure to increase the amount of fungistatic sebum which is normally found on the scalps after puberty. In his series, no toxic effects were noted. Although his results were encouraging, he failed to observe ultimate cures of ringworm from this procedure. He did however, observe that following the administration of undecylenic acid, an increase of sebaceous secretion and a profuse desquamation of the scalps occurred.

It was at this point that he conceived the idea of giving the fatty acids internally for the treatment of psoriasis. The easily obtainable unsaturated undecylenic acid was selected for his clinical research. The favourable results obtained in the treatment of 25 cases of psoriasis and neurodermatitis prompted Perlman[10] to publish a preliminary report of his findings.

No acute or chronic toxic effects have been found in experimental animals fed on undecylenic acid, nor has Perlman reported toxicity in the human subject maintained on an equivalent regimen. His rather large doses, ranging from 6 to 15 grams per day did, however, give some side effects which, by and large, were corrected when the dosage of the drug was reduced.

Undecylenic acid (10 undecenoic acid) is an eleven carbon straight chain unsaturated fatty acid ($CH_2CH(CH_2)8$ COOH). At higher room temperature (m.p. 24.5° C.) it is an oily water-insoluble liquid. It has a heavy characteristic somewhat objectionable fatty odour and a persistent acrid taste. It must be encapsulated for oral administration. It has no known source in common foodstuffs. It is produced by cracking of castor oil under pressure. Inasmuch as it is an odd-numbered fatty acid, it is assumed that the product would be broken down in the body in the same way as other odd-numbered fatty acids. However, as yet the exact metabolism is undetermined.

Dr. Wallace[11] of the Decyl Pharmaceutical Co., states that methods for determining qualitative-quantitative blood levels will be available in the near future, but, at the time of writing, these methods have not been released.

Pharmacologists advise that a purified type be used for internal administration, rather than the current form used for anti-mycotic topical applications. Further, it is suggested that an enteric-coated capsule would reduce the symptoms of gastric irritation. The commercial product, "declid", in soft gelatin capsules, each containing 0.44 grams, was used in this clinical investigation.

Late in March, 1949, we received our first limited supply of purified undecylenic acid capsules ("declid"). We then planned to ascertain if the drug could cause increased sebaceous gland secretion or gland hyperplasia as evidenced in histological sections. This investigation was abandoned early, due to the difficulty in obtaining sections of psoriatic, for comparison with adjacent normal skin. Our confrères in pathology felt that without a qualitative stain, no quantitative values could be obtained with this procedure. Further, microchemical analysis would have been interesting and perhaps valuable, but unfortunately, such procedures were not available in our hospital. Total lipid determinations were done on the blood of all patients prior to the giving of undecylenic acid and second levels were ascertained after periods of therapy. No significant changes were noted. As no stool fat estimations were done, we have no means of knowing how much fatty acid was absorbed during periods of therapy. This we hope to do at a later date.

Clinically, we compared the cutaneous changes occurring in our patients with those observed by Perlman. (1) Exfoliation of the scalp with increased amounts of sebaceous secretion. (2) Relief of itching. (3) Increased oiliness of whole skin surface. (4) Drying and shedding of the guttate lesions. (5) Softening of the indurated plaques.

Constitutionally we watched for toxic reactions which he noted, such as heart burn, gastric upsets with diarrhœa, as well as the untoward cutaneous response of folliculitis.

DOSAGE

The dosage schedule was arbitrarily set at 15 capsules a day (0.44 grams per capsule) and with some cases, where tolerance was good, this was increased to twenty capsules a day. On the advice of Samitz,[12] we have insisted that our patients take the gelatin capsules between meals, with water, and have suggested the use of baking soda if gastric distress occurs.

Thirteen males and nine females agreed to undergo oral undecylenic acid therapy for psoriasis. Of these, 17 were followed for periods varying from 30 to 120 days. All patients in the series had previously failed to permanently respond to various standard methods of therapy. The average duration of the disease in our series was 21 years and the average age was 44 years. With the exception of one whose lesions were confined to the scalp, all had a universal distribution of the skin lesions. Only two displayed nail involvement, but surprisingly, all complained of varying degrees of itchiness prior to taking the drug. This, we noted as an interesting observation, not usually recorded as a symptom of psoriasis.

As a placebo, patients were instructed to use only vaseline or cold cream as a skin lubricant. Two who came to us using local therapy were allowed to carry on with their ointments, while two others employed no local applications throughout the period of internal therapy.

OBSERVATIONS

In comparison with Perlman's findings we were not impressed with exfoliation of the scalp, which he has stressed. The majority of our cases had immediate relief from itching soon after the undecylenic acid was taken, but in four of the group the pruritus was intensified during the first thirty days of the oral undecylenic acid regimen. Our patients did not exhibit generalized oiliness of the skin after taking the medication.

Group 1.—Three cases displaying universal psoriatic lesions responded satisfactorily to therapy and all but a few minor patches disappeared within the two months' period.

Group 2.—In nine cases, benefits accruing from the administration of the undecylenic acid appeared to us to be equivalent to the usual response obtained from ambulatory topical therapy. In these cases we noted that the lesions became fewer, smaller, and displayed powdery, greasy and more easily detachable scales on the involved psoriatic skin. The Goeckermann treatment, which requires hospitalization, will still give more rapid results. It may be, however, that the undecylenic acid will give a more lasting relief.

Group 3.—In five cases, except for slight thinning and shrinking of the lesions, no other observable changes were noted.

COMPLICATIONS

1. *Cutaneous.*—Two cases in Groups 1 and 2 at the onset of therapy exhibited multiple new lesions on the body together with folliculitis on the extremities. Two additional cases displayed folliculitis alone. All four cases cleared within the second week on reduced dosage.

2. *Systemic.* — Toxic headaches occurred in three cases, but lasted only for a short period. Belching was a constant complaint, for the first week, from all patients. All but two tolerated the drug well; one of these suffered from an acute gastric upset with diarrhœa, which could well be explained on a history of previous gall-bladder disease. After six weeks of repeated attempts to take the capsules, this patient was forced to abandon therapy. The second patient experienced anorexia and diarrhœa which persisted even with reduction in dosage and finally had to discontinue therapy.

No exact evaluation of body weights before and after administration of the undecylenic acid was recorded. Statements of patients revealed an initial weight loss which occurred within the first two weeks—perhaps due to loss of appetite. This initial loss was soon regained.

Unanswered questions.—(1) What is the optimum dose and for what period should the drug be administered? (2) Will larger doses in excess of 10 gm. per day prove to be more efficacious? (3) Will a maintenance dose prevent exacerbations? (4) Will undecylenic acid in such large doses produce systemic complications?

SUMMARY

This study was conducted on a non-selected group of chronic psoriatics. We realize that psoriasis often spontaneously improves during the spring and summer months during which time these observations were made.

Undecylenic acid occasionally causes non-toxic yet unpleasant side effects and should not be administered to patients with a history of gastro-intestinal upsets.

We are sufficiently impressed with the results obtained in the treatment of psoriasis to continue with the internal administration of undecylenic acid, alone, and combined with topical therapy.

Acknowledgment is made to Mr. Harry Cohen of Capes Drug Store for his services in facilitating the receipt of declid capsules, generously supplied to patients by Dr. H. S. Wallace of the Decyl Pharmaceutical Co., Princeton, N.J.

REFERENCES

1. CONELLI, A. S.: Pædiatria, p. 33, 1925.
2. LANE, C. G. AND CRAWFORD, C. M.: *Arch. Dermat. & Syph.*, **35**: 1051, 1937.
3. GRUETZ, O. AND BUERGER, M.: *Klin. Wchnschr.*, **12**: 373, 1933.
4. GATE, J., CHANIAL, G., VALIET, A. AND HUMBERT, P.: *Ann. de dermat. et syph.*, **9**: 465, 1938.
5. ROSEN, ROSENFELD AND KASNOW: *Arch. Dermat. & Syph.*, **35**: 1093, 1937.
6. HERING, H.: *Dermat. Wchnschr.*, **106**: 109, 1938.
7. MADDEN, J. F.: *Arch. Dermat. & Syph.*, **39**: 268, 1939.
8. DRAGSTEDT, L. R., PROLASKA, J. AND HERMIS, H. P.: *Am. J. Physio.*, **117**: 175, 1936.
9. STEWART, C. D., CLARK, D. E., DRAGSTEDT, L. R. AND BECKER, S. W.: *J. Invest. Dermat.*, **2**: 219, 1939.
10. PERLMAN, H. H.: *J. Am. M. Ass.*, **139**: 444, 1949.
11. WALLACE, J. H.: Personal communication.
12. SAMITZ, M. H.: Personal communication.

PREFRONTAL LEUCOTOMY FOR PAINFUL PHANTOM LIMB

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IN the assessment of the severity and type of pain from which a patient is suffering, it is important to realize that pain has two elements. Firstly, there is the sensation of pain, travelling along well-defined pathways to the thalamus, at which level it reaches consciousness. Secondly, it is necessary to consider the reaction of the patient to pain, in terms of its meaning to him, and this varies with his ability to withstand threats to his person. This, in turn, is dependent on his emotional state. For example, an anxious patient will react more profoundly to a certain intensity of pain than one who is not so tense.[9]

A variety of surgical procedures has been carried out in the attempt to alleviate severe and intractable pain, and until recently, these have been aimed at interruption of the pain pathways below the thalamic level. Amongst these operations may be mentioned:

1. Infiltration with local anæsthetics or destructive agents, either around the focus or irritation, or proximally into or around the peripheral nerves supplying the part.

2. Surgical interruption of the peripheral nerves, either somatic or autonomic, supplying the part. This may involve division, resection, cautery, or other methods of attack, and periarterial stripping, pre- or post-ganglionic sympathectomy, sympathetic ganglionectomy, or a combination of several of these.

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3. Intrathecal injections of spinal anæsthetics or alcohol.
4. Posterior rhizotomy.
5. Myelotomy.—Incision of the posterior commissure in the vertical plane over a level of several segments.
6. Cordotomy.—Division of the lateral spinothalamic tract, either unilaterally or bilaterally.
7. Medullary tractotomy.

Excision of the appropriate area of the sensory cortex has also been carried out, as reported by Horrax,[2] and Livingstone,[3] but its efficacy has not been generally accepted. Moreover, Penfield and Boldrey[4] state that pain has little cortical representation.

None of these methods, alone or combined, can assure relief from pain, and it is not uncommon for several procedures of increasing severity to be carried out on the same patient. Thus, cases may graduate from the fairly simple procedure of local infiltration to the major operation of cordotomy. Many of these operations may be only temporarily successful, the analgesia obtained often tending to diminish at a later date with reappearance of the original pain, to a greater or lesser degree. This seems to indicate that painful stimuli may be able to find for themselves new pathways, by which to reach the thalamus.[3]

Although a large proportion of patients are undoubtedly cured of pain by one or more of these procedures, there remains a small percentage who still suffer from pain which may truly be described as intractable.

RÔLE OF LEUCOTOMY

Freeman and Watts in 1937, and more recently, Poppen,[5] Scarff,[7] and other neurosurgeons have shown that some hope of relief from intractable pain may be offered by the operation of prefrontal leucotomy.

That the division of the association fibres between the thalamus and the prefrontal region should not relieve pain, will be readily understood, as it is known that pain reaches the sensorium at the thalamic level. However, owing to the modification of the interpretation of painful stimuli which takes place in some regions of the prefrontal cortex, division of these fibres causes marked changes in the reaction to pain. The emotional factor is modified or obliterated completely, and the fear and foresight of pain is abolished.

This alteration in response has been discussed more fully by Freeman and Watts,[1] and is well-illustrated in the two cases herewith described.

Painful phantom limb.—Many theories, from peripheral nerve irritation in the stump, to neurosis, have been put forward to account for the symptoms of pain which may be produced by a phantom limb. Both Livingstone[3] and Riddoch[6] have pointed out that in most cases, both organic and psychological factors are involved, but the origin of the symptoms remains obscure. Undoubtedly the majority of cases have an emotional element, which influences the complaint of pain.

The following points may be mentioned in support of a central origin of the pain sensation: (1) The parts felt most severely in this syndrome are usually those with the largest representation in the sensory cortex, *i.e.*, hand and foot, etc. (2) There are no peripheral end organs present to account for the sensory impressions received. (3) In a large proportion of cases, the painful phantom limb is held in the position in which it was last remembered by the patient.

Opposed to these factors, may be mentioned the following facts, which tend to support a peripheral origin: (1) In many typical cases of painful phantom limb, revision of the stump, division of peripheral nerves, excision of neuromata, posterior rhizotomy or cordotomy gives relief. (2) Interruption of the autonomic nerve supply to the extremity may result in improvement or even cure of the symptoms, especially if there is added vasomotor dysfunction in the stump.

Thus, whilst the mechanism must be considered to be more than a simple irritation of peripheral nerve endings by scar tissue, or constriction of blood vessels in the local tissues, an entirely functional diagnosis cannot always be accepted.

Prefrontal leucotomy is defined as a division of the white fibre tracts between the prefrontal area and the remaining portion of the brain, and may be performed in the vertical, oblique, or horizontal plane. In both of the cases described, the technique of Freeman and Watts was used. The white matter was divided as completely as possible, with the patient under pentothal anæsthesia.

CASE 1

F.H., white male, aged 68. Amputation through the surgical neck of the right humerus had been performed on the 15th of February, 1945. This had followed a dislocation of the shoulder, and ligation of a resulting traumatic subclavian aneurysm, causing inadequate circulation in the right upper limb.

A very painful phantom limb developed, with the arm held adducted, the elbow bent with the forearm across the chest, and claw hand. Severe burning pain was experienced, especially in the hand and forearm. On

November 16, 1947, the symptoms were as described. There were irregular adherent scars over the site of amputation, with marked puckering of the skin. He was reluctant to allow palpation of the stump area. The brachial plexus was extremely tender, as were nerve endings in the stump. He wore a permanent expression of severe pain, although he was otherwise in good physical condition for his age. Repeated sympathetic blocks were performed, each time with temporary relief, but with ultimate return of the pain in all its former severity. Increasing amounts of sedation were necessary to control this patient's pain.

It was felt that an attempt at some permanent relief should be made and after due consideration, prefrontal leucotomy was considered to offer a reasonable prospect of success. This procedure, with its possible hazards, was fully explained to the patient and his family. They all willingly agreed to co-operate in any treatment that might be expected to offer him relief from pain. Prior to operation, this man had no gross memory defect. There was slight disorientation in the temporal sphere. He was not psychotic and had good insight into his emotional difficulties, admitting unreasonable irritability at home, particularly since he had been suffering pain.

On the morning of March 30, 1948, bilateral prefrontal leucotomy was performed. For the first two weeks after operation, he was confused. There was very little spontaneous speech, and no interest was shown in his environment. He spoke, but only in answer to questions. Answers were usually irrelevant. He appeared to be suffering no pain whatsoever. The latter part of the second week saw an improvement in his orientation, particularly as to place and person. In the temporal sphere, there was no improvement. For two weeks there was indifference as to where he voided, but subsequently, this was not manifest.

Intellectual function showed steady improvement, and five weeks postoperatively, it was considered that as far as memory, orientation, and general information went, he was practically at his preoperative level. Orientation in the temporal sphere had not recovered as well as that of the other spheres. He had recovered his preoperative façade, minus the signs which indicated that he was in pain. He was cheerful, talkative, and jocular. On June 4, this patient was discharged to his home, and at that time did not recognize that he had had an operation.

When last examined, six months later, he was entirely free from complaints of pain.

CASE 2

R.R.W., white male, aged 63. This patient complained of a painful mid-thigh amputation stump since 1929. He had always been aware of the absent foot, but this had not been painful and most of his complaints of pain had been centered locally in the stump. Several operative procedures had been carried out for the relief of the painful stump, with only temporary improvement.

Painful phantom limb symptoms began in 1946, with jabbing pain in the toe and heel of the amputated foot, and became increasingly severe. Sedation was required in increasing amounts, and he was hospitalized several times, on account of pain. Sympathetic blocks were performed with variable results. On May 9, 1948, he was again admitted to hospital, with severe pain in the phantom limb. He was begging for hypodermic injections, and during the next seven weeks, heavy sedation was given on occasions with little relief.

There were no points of local tenderness in the stump, no tender neuromata, no apparent vasomotor dysfunction, and, as he had previously undergone revision of the stump (1932) and cordotomy (1938) without relief, prefrontal leucotomy was decided upon. Intellectual functions at this time were considered to be well-preserved, and personality factors were not thought to be of a nature to preclude benefit from this operation.

In view of a recent report by Scarff[7] of the beneficial effect of unilateral prefrontal leucotomy in the relief of intractable pain, this procedure was carried out on the right side on June 29, 1948.

Immediately after operation, the patient was cheerful and co-operative with no complaints of his phantom limb. Intellectual functions were intact. Memory was good for recent and past events. Biography was given exactly as in the preoperative interviews, with the same dates and sequences. Postoperative events were remembered quite well. No unpleasant effects resulted from the operation. He was aware of, and responsive to, his environment throughout, and sphincter control was maintained. He was discharged to his home two weeks after operation, free from all complaints, and moving around very actively on crutches.

Six weeks later, he was re-admitted to hospital, again complaining of severe pain in the phantom limb. In view of the apparent failure of unilateral leucotomy to give any lasting relief, left-sided leucotomy was performed on August 27, 1948. This was followed immediately by a mild degree of confusion, and temporal disorientation. He did recognize people correctly, however, and was cheerful and talkative as usual, with no complaints of pain. Speech displayed the usual spontaneity.

Over-night, August 30 to 31, there was a marked change, and psychomotor activity was at a minimum. He knew his name but not his place of birth, where he was, or how long he had been here. He did not remember having had an operation. Responses to questions were sometimes irrelevant, and at other times, obviously offered as a guess. He showed no distress at his wrong answers.

Within a few days, he began to take some interest in his surroundings, got up and around in a wheel chair, and before long, on crutches. He took no sedation, asked for none, and complained of no pain. Discharge from hospital was effected on October 18.

Three weeks later, he was interviewed and found to be alert, co-operative and cheerful. On the whole, his appearance and manner showed no marked change from his preoperative façade. He had temporal disorientation, and memory defects, but these were not marked. The memory gaps were patchy and largely filled in by confabulation. He found his way about easily, recognized people and places, but was unable to give the date of his birth. When last examined, on February 2, 1949, he had no complaints of pain.

DISCUSSION

The two cases described are of elderly men who have been made miserable by constant, intractable pain from phantom limbs, and had been incapacitated from useful activity for several years. White[8] has pointed out that addiction to drugs is very liable to occur in such cases. Both of these patients had required increasing amounts of sedation in order to control their pain. Following bilateral prefrontal leucotomy, there has been entire freedom from complaints of pain. No sedation has been requested or prescribed.

The degree of improvement shown by these two veterans as a result of leucotomy is very striking, and it is felt that the last years of their lives have been made comfortable. It is noted, however, that unilateral prefrontal leucotomy failed to give lasting relief in the one patient on whom it was performed.

Whilst bilateral prefrontal leucotomy cannot be regarded as the ideal solution to the problem

of intractable pain in all its forms, it is considered that the operation has a definite field of usefulness in selected cases of painful phantom limb.

SUMMARY

1. Brief mention is made of some methods of treatment for intractable pain.

2. The rôle and effects of prefrontal leucotomy are outlined, and painful phantom limb is discussed.

3. Two cases are described illustrating the effects of prefrontal leucotomy on intractable pain due to phantom limb, and it is concluded that the operation may be of benefit in selected cases, where all other measures have failed.

REFERENCES

1. FREEMAN, W. AND WATTS, J. W.: *Ann. Int. Med.*, **28**: 747, 1948.
2. HORRAX, G.: *Surgery*, **20**: 593, 1946.
3. LIVINGSTONE, W. K.: Pain Mechanisms, Macmillan, New York, 1943.
4. PENFIELD, W. AND BOLDREY, E.: *Brain*, **60**: 389, 1937.
5. POPPEN, J. L.: *Lahey Clin. Bull.*, **4**: 205, 1946.
6. RIDDOCH, G.: *Brain*, **64**: 197, 1941.
7. SCARFF, J. E.: *J. Neurosurg.*, **5**: 288, 1948.
8. WHITE, J. C.: *J. Am. M. Ass.*, **124**: 1030, 1944.
9. WOLFF, H. G. AND WOLF, S.: Pain, Charles C. Thomas, Springfield, Ill., 1948.

DIABETES MELLITUS*

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IN a recent investigation of diabetes for life assurance purposes[1] a number of aspects were considered, in order to determine the extent to which it is now possible to control the condition. The group as a whole consisted of diabetics whom the writer had seen in his private office practice during the previous 25 years. The investigation was restricted to private patients for two reasons: Since private patients are more likely to follow treatment carefully than those who do not pay for their examinations, experiences with them afford a much more reliable index of the efficacy of any given form of treatment than experiences with charity patients. Also, as a group, private patients conform more with life assurance policyholders than charity patients.

General mortality.—The first, and obviously of prime importance from the standpoint of insurability, was the overall mortality, regardless of the causes of the deaths. For this purpose, one thousand diabetics were selected at random and grouped according to the degree of control of the diabetes. With this grouping, it was found that the ratio of actual to expected deaths amongst those in whom the diabetes was under good control was practically normal, that is, practically no more deaths had occurred amongst these diabetics during the period investigated than would have been expected amongst the same number of persons in a general population of non-diabetics with the same age-sex distribution. Other examples of the effectiveness of presently available methods of treatment were the experiences with coma, tuberculosis, gangrene, premature arteriosclerosis, diabetes in children and obesity.

Coma.—In 1914, the situation for the severe diabetic was tragic; if he did not follow treatment, he died from coma; if he followed treatment, he died from starvation. Coma then accounted for two-thirds of all the deaths. Now, with extremely few exceptions, it is inexcusable. In the entire group in this investigation there had been five such cases only during the previous five years and no deaths from it.

Tuberculosis.—Tuberculosis, which before the discovery of insulin was present in almost half of all of the fatal cases, was found no more common in this group than amongst the general population of non-diabetics.

Gangrene.—Amputation of legs for diabetic, gangrene, common in the past, with a very high mortality, had to be performed in three cases only in the entire group during the previous five years, and there were no deaths. Statistics are often difficult to interpret because of the many variables, but one of the simplest procedures in statistics is to count amputated legs and dead people.

Premature arteriosclerosis. — The data also clearly showed that the rule that premature development of arteriosclerosis is inevitable in cases of diabetes of five years' duration holds no more, provided treatment is followed carefully.

Juvenile diabetes. — Most encouraging had been the health of the diabetics who had developed the condition in childhood; who had followed treatment carefully and who, at the time of this investigation, were fully mature adults; though most disastrous had been the

* From an address delivered before the American Chemical Society, Atlantic City, September 23, 1949.

results amongst those who had not followed treatment carefully — blindness from diabetic retinitis, death from advanced nephritis and even coronary thrombosis at age 20 years.

Obesity. — Though, in general, excess body weight was a favourable sign at the onset of the diabetes, failure to reduce the excess weight resulted in loss of carbohydrate tolerance and in an increased mortality. In a group of 521 diabetics who had been over-weight at the onset of the diabetes, the highest ratio of actual to expected deaths was found amongst those who had failed to reduce their weights to the "best" weights for their heights according to life assurance company standards.

Improvement of carbohydrate tolerance. — A possibility which had to be investigated was whether, though the present mortality experiences may be satisfactory, there is an inherent tendency for the diabetes to become worse. If there is, a factor to consider is a "piling effect" —an ultimate death rate which would have to be allowed for in calculating the premium. Most gratifying, therefore, was the finding that, regardless of the severity of the disease, there is no evidence of an inherent tendency for the diabetes to become worse; that, in fact, provided treatment is followed carefully, there is an appreciable expectation of improvement of carbohydrate tolerance, so that an appreciable percentage of individuals who require insulin are expected to be able to discontinue its use eventually. Approximately, one-fourth of the diabetics in this entire group who had required insulin at the beginning of treatment had been able to discontinue its use.

Recent Studies of Anæmia and Neuritis in Diabetes

Anæmia.—But these advances do not warrant the conclusion that all of the problems of diabetes have been solved. More recently[2] the writer drew attention to the high incidence of achlorhydria amongst diabetics and its relation to anæmia and to neuritis. One of the functions of hydrochloric acid in the stomach is to liberate the iron in food materials from its organic combination; to convert the liberated iron into ferrous form and, by creating and maintaining the proper acidity in the upper part of the intestinal tract, to aid the absorption of the iron. A low free hydrochloric acid content of the stomach secretions has the opposite effect; hence the common occurrence of anæmia or cases on the borderline of anæmia in diabetes mellitus. Therefore, as was clearly shown, for the prevention of the anæmia in such cases or to treat that which may be present, in addition to the proper diet, for the control of the diabetes, an essential part of the treatment is administration of hydrochloric acid.

Neuritis.—Neuritis, though less frequent than anæmia, is by no means uncommon in diabetics, and one of the causes may be deficiency of vitaman B_1, but this is not to say that the diet of the diabetic is deficient in this vitamin and, therefore, that it is necessary to supplement the diet of the diabetic with it to prevent the neuritis. Vitamin B_1 is readily destroyed in alkaline media. There is also evidence that an alkaline secretion in the upper part of the intestines interferes with its absorption. It is, therefore, to be noted that, in the absence of free hydrochloric acid, not only may the acidity in the stomach be very low but the secretions may be actually alkaline. Therefore, for the prevention of neuritis in such cases or for the treatment of it, as in the case of anæmia, in addition to the proper diet for control of the diabetes, an essential part of the treatment is administration of hydrochloric acid. In the writer's experience, approximately 40% of diabetics have no free hydrochloric acid in their stomach secretions.

Utilization of Sucrose in Diabetes Mellitus

The chief purpose of this communication is to report the findings of a study of the utilization of sucrose by diabetics. It will be necessary here to outline briefly the developments which had prompted this investigation.

Historical.—Before the discovery of insulin, theories concerning the cause of diabetes centred very largely on the pancreas. The discovery of insulin strengthened these views. By 1930, however, evidence had been accumulating, in animals and in man, which pointed to causes other than defective insulin production by the pancreas.[3] By then, conditions capable of modifying the course of the diabetes, regardless of the cause, were also becoming increasingly recognized, and one was the composition of the diet, but the experiences in animal and in man were not the same. In animals, it had been found that carbohydrates depress production of insulin by the pancreas. According to this finding, the diet of the

diabetic should be very low in carbohydrates; but, in order to meet the caloric requirements, it would have to be high in fat, and this, in fact, was, with very few exceptions, the method of treatment then employed. In man, however, there was increasing evidence that, provided the blood sugar was kept at the normal level, carbohydrates actually increase carbohydrate tolerance, whereas, fats have the opposite effect. Because of these and a number of other experiences, an attempt was made by the writer to increase the carbohydrate contents of his diets. It was, however, still necessary to control the total caloric intake so as to avoid excess body weight. To do so, it was necessary to reduce the fat content to quite a low level. Eventually, a fairly standard procedure was arrived at and, in 1930, the writer[4] reported his experiences with what he termed a "high carbohydrate-low calorie diet", which, with a few modifications[5] he has employed since then. Proof of the effectiveness of this diet may be seen in the small percentage of diabetics who require insulin with it, compared with the percentages with all other diets; the smaller average dose, compared with the requirements with all other diets, and the percentage who have been able to discontinue its use entirely. Its beneficial effects otherwise—reduction of plasma cholesterol, improved protein metabolism, improvement of liver function, etc.—have been described since then.[5, 6]

An advantage of this diet is that, because of its liberal carbohydrate content, it permits such a variety of food materials that, except for the allowance of fat, it approximates very closely the normal food habits of the individual. For example, one of the units of the diet is a slice of bread three and one-half inches square and one-half inch thick. Such a slice of bread weighs about one ounce and contains about 18 grams of carbohydrate. Three average teaspoonfuls of table sugar also weigh about 18 grams. Therefore, if the diabetic wishes to have three teaspoonfuls of sugar for any purpose, all he need do is omit one slice of bread. This will not seriously detract from the diet, because, with a carbohydrate allowance of 200 to 300 grams per day, very few diets contain less than six slices of bread—two for each meal. Since 1930, therefore, many of these diabetics have been adding sugar to their tea or coffee and to foods otherwise. On the other hand, many, having lost the taste for sweets early in the course of their treatment because of previous diets, have not been taking advantage of this substitution. As the result of these experiences, therefore, and others to be referred to later, it had been the writer's impression for some time that sucrose is not merely useful as a source of calories and as a sweetening agent, but that it has an influence upon the metabolism of the diabetic which cannot be accounted for by its dextrose and lævulose fractions only or, at least, by dextrose and lævulose in their presently known forms; but impressions are not facts. To test this impression, therefore, an investigation was started in 1944, and, from the data—comparison of the effects of sucrose with those of dextrose alone, lævulose alone and stoichiometric mixtures of dextrose and lævulose (7.8)—it seemed clear that the metabolism of sucrose in man cannot be accounted for by the metabolism of dextrose and lævulose only.

Experimental.—Because of these experiences, an attempt was made to determine whether sucrose has nutritional properties which carbohydrates of foods which do not yield sucrose do not possess. One of the procedures was to determine whether, in human diabetes, the tolerance of sucrose differs from the tolerance of carbohydrates of such foods as bread, and the purpose of this communication is to report the results.

Selection of experiments.—For this study there were two choices of experiments, namely, (*a*) a short-period experiment with a small number of subjects in which food materials would be weighed accurately in order to determine the carbohydrate intake and (*b*) a mass-feeding experiment over a long period of time in which the intake of food would, for practical reasons, have to be approximated.

The short-period experiment in a small number of subjects was immediately excluded, because of the uncertainty of the actual intake of carbohydrates, regardless of the accuracy with which the foods would be weighed, due to the natural, and at times marked, variations of the carbohydrate content of food materials. For example, 30 grams of potato are generally assumed to contain 6 grams of utilizable carbohydrate. Actually, a random sample may contain as much as 9 grams or as little as 3 grams. On the other hand, it can be shown by analysis

that, if taken daily over a long period of time—one month or more—30 grams of potato correspond almost exactly to an intake of 6 grams of carbohydrate.

For the mass-feeding experiment over a long period of time, therefore, the only remaining consideration was the extent to which approximation of food weights would affect the accuracy of the intake. That here also the long duration of the experiment assures the necessary accuracy may be seen from actual measurements. Provided the unit of measurement is adhered to reasonably carefully a greater intake one day is counterbalanced by a lesser the next. In any case, the possible errors are not additive; in any given experiment involving two or more measurements each of which has its own error, the final error is not equal to the sum of the individual errors but to the square root of the sum of their squares. It was for these reasons that, in 1925, the writer found that, provided the patients adhered to the simple units of measurements outlined, the diabetes could be kept under good control without subjecting them to the inconvenience of use of scales.[9] None has used scales since then.

TABLE I.

ACTUAL AND ESTIMATED WEIGHTS OF THREE APPROXIMATELY LEVEL TEASPOONFULS OF SUCROSE

Test	*Exp. 1*	*Exp. 2*	*Exp. 3*	*Exp. 4*	*Exp. 5*
1	22.2*	18.0*	17.5*	17.0*	20.1*
2	17.3	18.5	17.1	18.6	13.2
3	18.8	19.4	21.3	18.0	21.3
4	16.4	18.5	16.8	18.7	23.5
5	20.0	18.3	18.2	18.7	16.8
6	18.3	19.1	19.1	18.2	17.6
7	18.0	21.1	20.4	17.1	20.1
8	17.8	20.0	15.3	21.3	20.9
9	19.2	17.6	19.2	20.1	18.0
10	19.4	18.2	20.1	19.2	18.7
Average....	18.7	18.9	18.5	18.7	19.0

*Grams

In this experiment, for example, for every three teaspoonfuls of sugar desired, the subjects were to omit one slice of bread. The slice of bread, as stated, is three and one-half inches square and one-half inch thick. Bread, however, as is well known, may vary widely in texture so that such a slice may, at times, weigh appreciably less than one ounce and, at times, more. Actual analysis will, however, show that, over long periods of time—one month or more—the daily consumption of such a slice of bread corresponds almost exactly to a daily intake of 18 grams of carbohydrate, and the same accuracy is attained with the three teaspoonfuls of sugar. In any one measurement, three teaspoonfuls of sugar may weigh appreciably more than 18 grams of carbohydrate or appreciably less. Over a long period of time, however, three teaspoonfuls of sugar will weigh almost exactly 18 grams. This is shown in Table I, in which are recorded five different experiments, each of which consisted of ten measurements of three teaspoonfuls of sugar. It will be noted that in every one of the experiments, the average of ten measurements was almost exactly 18 grams; whereas, the mass-feeding experiment was to extend over periods of no less than six months and as long as three years.

Selection of subjects.—For this purpose, one thousand diabetics were selected at random, except for the conditions to be stated. Also, without exception, all had been under treatment for some time with the high carbohydrate-low calorie diet, which, because of its liberal carbohydrate content, permitted substitution of 20 to 80 grams of sucrose per day for corresponding amounts of carbohydrate in bread for periods of from six months to three years, without interfering with the necessary variety of foods in the diets. In view of the difficulty of interpreting changes of carbohydrate tolerance in mild diabetics, the subjects included only those in whom the diabetes had reached the stage at which quantitative diets were essential in order to keep the diabetes under good control. The selection was also such that, in addition to the quantitative diets, one-half required insulin.

In order to reduce the variables as much as possible, the selection was also such that the average carbohydrate content of the diets of those who used sucrose and that of the control group were approximately the same. For the same reason, the average period of observation was also approximately the same.

Amongst any group of one thousand diabetics, as amongst any one thousand people in general, deaths during such a period as employed in this investigation are inevitable. For this study, however, none was to be excluded, provided the person had been under observation for no less than the minimum period of six months. In fact, in the group as a whole there were 21 deaths. Four only of these persons, however, had to be replaced by others so as to have an exactly equal number of subjects

in each group. As the ratio of actual to expected deaths amongst those who had and those who had not made use of the sucrose substitution was practically the same, the findings about these deaths are irrelevant here.

Criteria of alteration of carbohydrate tolerance.—(*a*) *Non-insulin group*: Amongst those who had not taken insulin, the majority, as will be seen later, were on the borderline, that is, as a rule, the blood sugar was moderately increased. Periodically, the blood sugar was quite appreciably increased. Therefore, in this group, the criterion of a greater tolerance of sucrose than of the carbohydrate of bread was reduction of the average control index[10] (calculated from blood sugar values) to a definitely lower level than that of the control group. The significance of the difference was judged by

TABLE II.
CARBOHYDRATE CONTENT OF DIETS

Carbohydrate (grams)	*Number of cases*			
	Insulin		*No insulin*	
	Sucrose	*No sucrose*	*Sucrose*	*No sucrose*
218	15	16	20	18
236	29	29	42	54
254	74	89	88	63
272	95	83	57	70
290	24	23	34	28
308	13	10	9	17
Avge. gm.	262.8	261.0	258.8	260.2
S.D.	20.9	20.4	22.1	23.6
P.E.M.	0.89	0.86	0.94	1
D.	1.8		1.4	
P.E.D.	1.24		1.37	
D./P.E.D.	1.45		1.02	

S.D. = Standard deviation.
P.E.M. = Probable error of mean.
D. = Difference between means.
P.E.D. = Probable error of difference.

the ratio of the difference to its probable error. Proof of loss of carbohydrate tolerance was the percentage of individuals who had to have insulin at a later date, regardless of the number of units, compared with the percentage in the control group.

(*b*) *Insulin group*: The criteria of improvement of carbohydrate tolerance in the insulin-treated group were (1) the average reduction of insulin dosage, compared with that of the control group and (2) the percentage of those who were able to discontinue its use entirely, compared with the control group. Proof of loss of carbohydrate tolerance was the percentage who had to increase the insulin dosage, regardless of the number of units, compared with that in the control group.

Total carbohydrate intake.—In Table II are summarized the carbohydrate contents of the standard diets of different groups. It will be noted both in the insulin and in the non-insulin group that the average number of grams of carbohydrate was practically the same amongst those who had substituted sucrose for part of the bread allowance as amongst those who had not. This, however, as stated, was not accidental but the result of selection so that the data would be comparable as much as possible with regard to total carbohydrate intake. That the slight difference in each group was not significant is clearly seen by the ratio of the difference to its probable error.

TABLE III.
DURATION OF OBSERVATION
(MONTHS)

Duration (months)	*Number of cases*			
	Insulin		*No insulin*	
	Sucrose	*No sucrose*	*Sucrose*	*No sucrose*
7–12	30	36	46	50
13–18	50	39	53	48
19–24	45	57	47	54
25–30	61	56	50	49
31–36	64	62	54	49
Avge. period (months)	23.3	23.1	21.9	21.5

Duration of observation.—Table III shows that the data of the different groups were similarly comparable with respect to the average period of observation. This also, as stated, was not accidental but the result of selection so that the data would be comparable as much as possible in this regard. It will be noted that no subject was included who had not been under observation for at least six months; that the

TABLE IV.
AMOUNT OF SUCROSE

Sucrose	*Number of cases*		*No insulin*
	Insulin		
20	84		98
40	86		107
60	71		39
80	9		6
Average grams	40.32		37.20
S.D.	17.5		15.6
P.E.M.	0.74		0.66
D.		3.12	
P.E.D.		0.99	
D./P.E.D.		3.14	

S.D. = Standard deviation.
P.E.M. = Probable error of mean.
D. = Difference between means.
P.E.D. = Probable error of difference.

maximum was three years, and that the average over twenty months.

Sucrose intake.—In Table IV are shown the quantities of sucrose which had been taken. It will be noted that they ranged between 20 to 80 grams per day. The average appears to be almost the same in the insulin and non-insulin groups, but that it was definitely greater in the insulin group, that is, amongst the more severe diabetics, may be seen from the ratio of the difference to its probable error.

TABLE V.
INFLUENCE OF SUCROSE UPON CONTROL INDEX

		Control index				
Group	*No.*	*0*	*1*	*2*	*3*	*Avge.*
Whole	7418	44*	958*	4538*	1878*	2.11
Insulin	4111	35	520	2789	767	2.04
Sucrose	2122	13	236	1437	436	2.08
No sucrose	1989	22	284	1352	331	2.00
No insulin	3307	9	438	1749	1111	2.20
Sucrose	1685	6	109	941	629	2.30
No sucrose	1622	3	329	808	482	2.09

*Number of tests.

Influence of sucrose upon degree of control of diabetes.—The first step in this investigation was to determine the degree of control of the diabetes in the four groups shown in Table II, according to the control index.[10] For this purpose, as Table V shows, there were 7,418 blood sugar determinations, and no control index was calculated from less than 1,500.

That the sucrose was tolerated better than the corresponding amount of carbohydrate in bread is suggested from the finding that, regardless of the severity of the diabetes—whether the subjects did or did not require insulin—the average control index was higher amongst those who had used sucrose than amongst the control group. In the insulin group, the average control index of those who had used sucrose was 2.08; whereas, in the control group, it was 2.00. In the non-insulin group, the values were 2.30 and 2.09 respectively. That the difference in each case was significant may be seen in Table VI from the ratio of the difference to its probable error.

TABLE VI.
INFLUENCE OF SUCROSE UPON CONTROL INDEX

	Insulin		*No insulin*	
	Sucrose	*No sucrose*	*Sucrose*	*No sucrose*
No. of tests	2122	1989	1685	1622
Avge. index	2.08	2.00	2.30	2.09
S.D.	0.58	0.59	0.60	0.71
P.E.M.	0.0084	0.0088	0.0097	0.0118
D.	0.08		0.21	
P.E.D.	0.012		0.015	
D./P.E.D.	6.6		14.0	

S.D. = Standard deviation.
P.E.M. = Probable error of mean.
D. = Difference between means.
P.E.D. = Probable error of difference.

Insulin requirements.—If sucrose is, in fact, tolerated by the diabetic better than a corresponding amount of carbohydrate in bread, *a priori,* one would expect, after an average period of over twenty months, not only a definitely greater reduction of insulin dosage, but also a greater percentage who would be able to discontinue the insulin, than in the control group. In Table VII are, therefore, shown (*a*) average insulin dosages at the beginning and at the end of the period of observation amongst those who had used sucrose as a substitute and amongst those who had not and (*b*) the number of individuals who had been able to discontinue the insulin in the two groups.

TABLE VII.
INSULIN REQUIREMENTS

	Sucrose		*No sucrose*	
Insulin (units)	*At beginning*	*At end*	*At beginning*	*At end*
10	17	30	17	31
15	26	36	39	38
20	54	46	37	26
25	16	10	17	10
30	20	15	29	24
35	30	9	19	16
40	17	4	29	13
45	19	5	16	3
50	8	2	8	6
55	8	3	13	9
60	13	3	11	6
65	8	3	6	7
70	4	1	4	2
75	2	3	1	—
80	6	—	3	—
85	—	—	—	—
90	2	—	1	2
95	—	1	—	—
100	1	—	—	1
Total No.	250	171	250	194
Avge. units	34.2	24.2	32.7	28.9

It will be noted that, whereas, at the beginning of treatment, the average dose amongst those who had used sucrose was 34.2 units and at the end it was 24.2 units, amongst those who had not used sucrose, the values were 32.7 to 28.9 respectively. This Table also shows that, whereas of the 250 who had used sucrose, 79 had been able to discontinue the insulin—an incidence of 31.6%, amongst the 250 in the control group, 56 only—an incidence of 22.4% —were able to do so.

That the average reduction of the insulin dosage was much more significant in the sucrose

than in the control group may be seen in Table VIII, in which is recorded in each case the ratio of the difference to its probable error.

Additional evidence of greater tolerance of sucrose than the corresponding amount of carbohydrate in bread is seen in Table IX in which the average control index of the sucrose group is compared with that of the control group, amongst the individuals who were able to discontinue the insulin. It will be noted that whereas, in the sucrose group, it was 2.35, in the control group it was 2.25. That this difference, though it may appear slight, was also significant may be seen in Table X, in which is recorded the ratio of the difference to its probable error.

TABLE VIII.

INSULIN REQUIREMENTS

	Sucrose		*No sucrose*	
	At beginning	*At end*	*At beginning*	*At end*
No. of cases	250	171	250	194
Avge. units	34.2	24.2	32.7	28.9
S.D.	25.8	15.7	17.1	18.1
P.E.M.	1.09	0.80	0.73	0.87
D.	10.0		3.8	
P.E.D.	1.35		1.29	
D./P.E.D.	7.4		2.9	

S.D. = Standard deviation.
P.E.M. = Probable error of mean.
D. = Difference between means.
P.E.D. = Probable error of difference.

TABLE IX.

CONTROL INDEX IN CASES IN WHICH INSULIN WAS DISCONTINUED

		Control index				
	No.	*0*	*1*	*2*	*3*	*Avge.*
Insulin discontinued	1046	0*	117*	485*	444*	2.31
Sucrose	626	0	72	261	293	2.35
No sucrose	420	0	45	224	151	2.25

*Number of tests.

Loss of carbohydrate tolerance.—In any large group of diabetics, loss of carbohydrate tolerance is to be expected in an appreciable percentage of cases for different reasons—dietary indiscretions, etc. As stated, therefore, one of the criteria of loss of carbohydrate tolerance was to be the percentage of individuals who, though they were able to control the diabetes reasonably satisfactorily without insulin at the beginning of the period of observation, had to have it later. Therefore, further suggestive of a better tolerance of sucrose than of carbohydrate in bread is seen in Table XI in which are recorded the percentages of the subjects who required quantitative diets only at the beginning, but who required insulin later, in order to control the diabetes. It will be noted that, whereas, in the sucrose group, 14% only eventually required insulin, in the control group, 23.2% eventually required it.

TABLE X.

CONTROL INDEX IN CASES IN WHICH INSULIN WAS DISCONTINUED

	Sucrose		*No sucrose*
Number of tests	626		420
Average index	2.35		2.25
S.D.	0.68		0.63
P.E.M.	0.018		0.021
D.		0.10	
P.E.D.		0.028	
D./P.E.D.		3.57	

S.D. = Standard deviation.
P.E.M. = Probable error of mean.
D. = Difference between means.
P.E.D. = Probable error of difference.

DISCUSSION

Combining all of the findings, the evidence seems clear that the diabetic can tolerate sucrose better than the carbohydrate in bread. It is of interest to note here that, years ago, Greely, Tyler and Drury[11] found that definitely more sucrose than dextrose was tolerated by depancreatized dogs, though, according to Bollman and Mann,[12] apparently temporarily only. More relevant here was the early observation by Joslin[13] that, in a mild diabetic, the respiratory quotient following administration of sucrose rose to as high a level as in normal subjects.

TABLE XI.

SHOWING INCIDENCE OF CASES ON QUANTITATIVE DIETS ONLY AT BEGINNING OF TREATMENT WHICH REQUIRED INSULIN SUBSEQUENTLY

	Number of cases at beginning	*Non-insulin to insulin*		
		Number	*Per cent*	*Average period**
Sucrose	250	35	14.0	21.9
No sucrose	250	58	23.2	21.5

*Months.

It is a well-known fact that the hyperglycæmic response to ingestion of lævulose is very much less than to ingestion of dextrose. Therefore, a possibility which had to be considered was that the greater tolerance of sucrose is due to its lævulose fraction. Experiences with lævulose feedings, however, before the days of insulin clearly showed that

the increased utilization of lævulose by the diabetic was temporary only; within a short time, the hyperglycæmic and glycosuria became as marked as with similar quantities of dextrose. The chief reason that artichokes were tolerated better than lævulose was that, though inulin, the chief carbohydrate constituent of artichoke, yields lævulose on hydrolysis, it is not readily hydrolyzed in the human body. The findings in this mass-feeding experiment, therefore, combined with those of the previous studies[7, 8] still further strengthen the view that the metabolism of sucrose cannot be accounted for by the metabolism of dextrose and lævulose only or at least by dextrose and lævulose in the forms in which they are known. Because of these findings, other possible effects of sucrose upon nutrition are now being investigated.

SUMMARY

Evidence is presented showing that the diabetic cannot only tolerate more sucrose than the carbohydrate of bread but that substitution of sucrose for corresponding amounts of such carbohydrate of bread results in improvement of carbohydrate tolerance, as shown by the average reduction of insulin dosage and the percentage of individuals who were able to discontinue the use of insulin entirely, compared with the control group. That the difference of metabolism of sucrose is not due to its lævulose fraction is suggested from previous experiences with feeding of lævulose. The combined data thus further support the view that the metabolism of sucrose cannot be accounted for by dextrose and lævulose only or at least dextrose and lævulose in its presently known forms.

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REFERENCES

1. RABINOWITCH, I. M.: *Am. J. Dig. Dis.*, **16**: 95, 1949.
2. *Idem*: *Am. J. Dig. Dis.*, In press.
3. LAZAROW, A.: *Physiol. Rev.*, **29**: 48, 1949.
4. RABINOWITCH, I. M.: *Canad. M. A. J.*, **23**: 489, 1930.
5. LOVELL, E. M. AND RABINOWITCH, I. M.: *J. Nut.*, **18**: 339, 1939.
6. RABINOWITCH, I. M.: *Canad. M. A. J.*, **58**: 547, 1948.
7. *Idem*: *J. Nut.*, **29**: 99, 1945.
8. *Idem*: *Am. J. Dig. Dis.*, **14**: 315, 1947.
9. *Idem*: *Canad. M. A. J.*, **15**: 1106, 1925.
10. *Idem*: *Ann. Int. Med.*, **8**: 1436, 1935.
11. GREELY, P. O., TYLER, D. B. AND DRURY, D. R.: *Proc. Soc. Exp. Biol. & Med.*, **41**: 36, 1939.
12. BOLLMAN, J. L. AND MANN, F. C.: *Am. J. Physiol.*, **107**: 183, 1934.
13. JOSLIN, E. P.: The Treatment of Diabetes Mellitus, 3rd ed., p. 299, Lea & Febiger, 1923.

TRAUMATIC CHYLOTHORAX

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LESIONS of the thoracic duct are among the rarer types of surgical lesions found in practice. The majority of cases of rupture of the thoracic duct found in the literature have been those associated with operative procedures about the neck, malignant changes in the wall of the duct or blockage from other causes. The complications arising from mediastinal rupture of the thoracic duct are chylothorax, inanition, with a mortality of 53% or superficial loss of chyle on the surface if the injury is in the cervical portion of the duct. The case to be presented is one in which the main thoracic duct was completely severed at the level of the eleventh dorsal vertebra by a .22 bullet in a hunting accident, followed by continuous chylothorax and rapid deterioration of the patient, in which the more conservative treatment of aspirations and dieting was of little value.

RESULTS OF INJURY TO THE THORACIC DUCT

A true chylothorax, first described by Bartolet in 1633, is one in which the fluid contains fat droplets (as high as 4%). It must be differentiated from a chyloform effusion secondary to tuberculosis or new growths. These latter fluids contain pus and endothelial cells undergoing fatty degeneration. Differentiation should also be made from pseudochylous fluid as seen in cardiac disease, amyloid disease, nephritis and leukæmia. The appearance of pseudochylous fluid is due to phosphates, cholesterol and lecithin. Prior to 1918 E. H. Funk found only 54 cases of chylothorax reported in the literature and since that time 45 more cases have been added. No reference is made of surgical repair or ligation of the thoracic duct until recent months.

Following the severance of the thoracic duct along its intrathoracic portion there is a stage of shock from the injury. After anti-shock therapy the patient frequently feels improved for two or three days except for extreme thirst and hunger. This may be considered the

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second stage. Following this stage there is generally a dramatic change and the patient becomes critically ill. He suddenly becomes weak, frequently semi-conscious, gasping for air and drenched in a cold sweat. He may be pallid or slate blue in colour and he lies motionless with half closed glassy eyes, the pulse is racing, thready and weak. The urine is scanty and loaded with acetone bodies. This sudden change is associated with the clear flow of chyle into the thoracic cavity and would appear to act in an anaphylactic manner; this is considered stage three. The first chest aspirations may reveal blood only or serosanguinous fluid, but, following the second stage, chyle is generally found. The results of traumatic rupture of the thoracic duct may be disastrous through loss of chyle and cause the patient to die of inanition as in a case of profuse chylorrhœa. There is marked thirst, progressive loss of weight and strength, cyanosis and collapse. This latter is considered as stage four.

Therefore we may have four distinct stages in traumatic chylothorax, each one being important and worthy of careful study. (*a*) Stage of shock as a result of the accident. (*b*) Stage of recovery and latent period of pleural effusion. (*c*) Stage of profound collapse from flow of chyle into the thoracic cavity acting in a manner to produce anaphylactic shock. (*d*) Stage of asthenia and inanition leading to death or recovery; the former from suffocation and heart failure or inanition, the latter from a sufficient collateral circulation or healing of the fistula.

In reviewing the literature we could find very little encouragement in the way of surgical treatment for a lesion of the thoracic duct along its course in the posterior mediastinum, much less at the level of the eleventh dorsal vertebra. References were made to lesions in the neck where pressure and ligation were considered in the treatment, but other than aspirations for chylothorax the literature was unavailable on curative treatment. Doubtless such cases have been met with previously and treated successfully, especially in the military services. As the case to be presented required some means of stopping the rapid loss of chyle through the rupture of the duct, a procedure was carried out which was successful, following a three weeks' period of the usual dietary and aspiration regimen during which time the patient was daily losing ground.

CASE REPORT

Mr. L.B., aged 30. This hunter was accidentally shot with a .22 rifle bullet through the right chest on the morning of September 23, 1947. The bullet, fired from a distance of twenty feet, entered the chest 1 cm. medial to the right nipple and was reflected off the body of the eleventh dorsal vertebra to lodge in the left psoas muscle.

Upon admission to the University of Alberta Hospital, following a trip of two hundred miles by truck, the patient complained of severe pain in the lower right chest, in the upper left quadrant of the abdomen and left costovertebral angle. Functional inquiry did not reveal any lesion pertaining to the gastro-intestinal or genito-urinary systems. He was apprehensive, slightly cyanosed and breathing with short, rapid respirations. He was free of pain as long as he was perfectly quiet and did not cough or breathe deeply. There was some decrease in movement on the right side of the thorax with the accessory muscles of respiration functioning. No breath sounds were audible over the right chest except at the apex. There was dullness on percussion over right chest to the level of the 5th rib posteriorly.

Except for a mediastinal shift to the left no abnormalities were detected in the heart. Blood pressure was 120/84, pulse 88, respiration 28. The temperature was 100.1° F. The abdomen was flat and moved with respiration. There was muscle guarding and tenderness with a rebound pain over the left upper quadrant upon palpation. The abdominal findings subsided after a forty-eight hour period.

PREOPERATIVE SEQUENCE OF ASPIRATIONS

September 24, x-ray of right lung showed it to be completely opaque by fluid.

September 25.—Aspiration of 1,200 c.c. of serosanguinous fluid.

September 26.—Aspiration of 570 c.c. of serosanguinous fluid.

September 27.—Aspiration of 2,100 c.c. of serosanguinous fluid.

September 29.—Aspiration of 975 c.c. of serosanguinous fluid.

September 30.—Aspiration of 1,200 c.c. of blood tinged fluid.

October 1.—Aspiration of 1,200 c.c. of blood tinged fluid.

October 2.—Aspiration of 1,000 c.c. of chyle.

October 3.—Aspiration of 1,280 c.c. of chyle.

October 4.—Total protein (blood) 5.6 gm. %, albumin 2.5 gm. %, globulin 3.1 gm. %, 1,500 c.c. of plasma given intravenously.

October 7.—Aspiration of 2,040 c.c. of chyle.

October 8.—Aspiration of 1,800 c.c. of chyle.

October 10.—Aspiration of 2,400 c.c. of chyle 1,000 c.c. of plasma given intravenously.

October 11.—Aspiration of 3,900 c.c. of chyle. The patient became cyanosed and complained of severe right chest pain for one hour following the aspiration.

October 12.—Aspiration of 3,000 c.c. of chyle. The patient again showed cyanosis, weakness and shock, with severe chest pain following the procedure. Blood pressure 104/60, pulse 94, respiration 28; 1,500 c.c. of plasma were given intravenously with improvement. Due to the gradual deterioration of the patient operation was performed. Under intratracheal anæsthesia, administered by Dr. Raymond Burnap an anterolateral incision was made over the line of the 9th rib on the right side. The 9th rib was exposed and removed, and the 10th and 8th ribs were sectioned beyond their angles and at their cartilages. The pleura was opened. There was a pneumothorax with approximately 16 oz. of chyle present with considerable fibrinous exudate attached to the diaphragm and also numerous white fibrous nodules on the diaphragm measuring approximately 4 mm. in diameter. The wound of the middle and lower lobes

was healed and did not necessitate repair. Following the suctioning off of the chyle it was found that the base of the right upper lobe was attached by fibrovascular adhesions to the site of the entry of the bullet, which was in the 4th interspace. There were also adhesions of the cardiac lobule of the lower lobe to the pericardium. These adhesions were ligated and cut. Retractors were placed so that good exposure was obtained of the area behind the heart at the level of the eleventh dorsal vertebra. The flow of chyle could be readily seen oozing at the level of the eleventh dorsal vertebra to the right of the aorta and posterior to the œsophagus between the azygos and hemiazygos veins. The inferior vena cava was retracted anteriorly and the remaining chyle suctioned off. Because of the difficult site of the lesion considerable time was taken in obtaining a satisfactory exposure of the 1 cm. chylous fistula. This, however was obtained and after the thoracic duct was dissected down to the fistula a number 1 silk suture was passed above and below the site, and a satisfactory closure was obtained. In order to ensure further security of closure a silk suture was passed widely anterior to the eleventh dorsal vertebra with its tissues, so that the duct would be again caught by the suture with more tissue protection. It was considered best to infiltrate the area of damage with ½ c.c. of 5% sodium morrhuate in order to cause sufficient reaction in this area to increase the fibrosis and further secure closure of any minute accessory tributaries of the duct. Following this fibrofoam was placed over the operative site in the posterior mediastinum, closure of the mediastinal pleura was carried out, the lung was inflated and the thorax closed in the usual manner following the instillation of 100,000 units of penicillin. The patient left the operating room in satisfactory condition.

The patient made a rapid recovery requiring one aspiration of 200 c.c. of serosanguinous fluid and was discharged from the hospital on October 22, 1947, ten days postoperatively. Two recalls at the office found the patient well.

During the investigation of the site of trauma it was found that the aorta, inferior vena cava, the œsophagus and the vena azygos escaped damage. This is strange because of the very close proximity of the structures to the track of the bullet which is at present lying symptomless in the left psoas muscle. Another centimeter either way would surely have severed the aorta or inferior vena cava with rapid death.

SUMMARY

1. A case of a traumatic chylothorax from a bullet wound at the eleventh dorsal vertebra is presented.
2. Successful treatment by ligation was carried out.

ADDENDUM

Since completing this paper one of the authors (W.C.W.) wishes to add another such instance. This is a case of a ten year old female on whom the author performed Blalock's operation for the tetralogy of Fallot. During the procedure of severing the vertebral artery the thoracic duct was damaged inadvertently, but as there was no evidence of it at the time the thorax was closed following the operation. Three days later it was evident that there was a chylothorax which required aspiration of 1,800 c.c. every other day. This treatment was continued for two weeks without any benefit. The thorax was opened at the first left interspace and the fistula of the thoracic duct readily detected. The thoracic duct was ligated in a similar manner as the previous case reported and also a good inspection was obtained of the Blalock anastomosis (subclavian artery to the pulmonary) which was functioning. Since the repair of the thoracic duct the patient has made an uneventful recovery and was discharged from the hospital ten days following the second operation.

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REFERENCES

1. GRANT, J. C. B.: Method of Anatomy, 3rd ed., Williams & Wilkins Co., Baltimore, 1944.
2. FLORER, R. AND OCHSNER, A.: *Surgery*, 17: 622, 1945.
3. BLALOCK, A.: *Arch. Surg.*, 34: 1049, 1937.
4. WHITCOMB, B. B. AND SCOVILLE, W. B.: *Arch. Surg.*, 45: 747, 1942.
5. BALDRIDGE, R. R. AND LEWIS, R. V.: *Ann. Surg.*, 128: December, 1948.

LEBER'S HEREDITARY OPTIC ATROPHY IN A CANADIAN FAMILY*

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ALTHOUGH several hundred families with Leber's hereditary optic atrophy have been reported from Europe and Japan, few families have been reported from the North American continent, and it seems that the one to be described here is the first to reach the literature from Canada. The family is unique because it is the largest yet to be reported, and because a pedigree to six generations can be plotted.

The character and the time relations of Leber's optic atrophy often resemble the retrobulbar neuritis that occurs so frequently with multiple sclerosis. They are more reminiscent, however, of the visual failure that occurred in some of our soldiers who were imprisoned by the Japanese during the second World War. Their failing vision came on gradually but often led to permanent impairment with optic atrophy and central scotoma.[1, 2] There is reason to believe that nutritional deficiency was responsible. This might be a lead to widespread preventive health measures for a family susceptible to hereditary optic atrophy. We are happy to say that the Department of Health and Welfare of the Dominion Government has undertaken a long-term and comprehensive study of this afflicted family and that they plan a positive nutritional experiment. Hereditary disease of

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this sort is probably but a lack, or mismating, of essential genes (enzyme systems) and therefore may some day be amenable to replacement therapy.

REVIEW OF LITERATURE

Hereditary optic atrophy is a condition in which the tendency to develop optic atrophy is inherited, visual acuity being normal until its onset. According to Julia Bell[3] the condition occurs predominantly in males (84.8% in 1,018 cases) and is generally transmitted by unaffected females. The average age of onset amongst males is 23 years and usually occurs without any obvious precipitating factor. Loss of visual acuity may be rapid, as with retrobulbar neuritis, or it may develop slowly over several months. Sometimes it may come on severely almost overnight and then progress more slowly. Early and rapid recovery, as seen sometimes with retrobulbar neuritis, does not often occur, but slow, delayed recovery is not uncommon. In some patients considerable recovery takes place but a central scotoma, which is the typical visual field defect for the condition, may remain. Peripheral vision may be retained, and then the patient may see better in subdued light than in bright light. In the early stages the optic discs may be suffused and show blurring of the margins. The vessels may be congested and tortuous and, rarely, small hæmorrhages may occur. Later, white discs with clear-cut edges of optic atrophy are found.

Probably the first cases to reach the literature were three patients with optic atrophy in one family, reported by von Graef[4] in 1858. Leber's name is attached to the disease in recognition of his classical description of the condition in 1871.[5] Since then there have been many reports of Leber's disease from scattered locations, indicating that there is no racial predilection.

Much of the interest in Leber's disease is centred around the material it provides for genetic studies. We should not look upon these matters with pessimism since there is now abundant proof that many hereditary diseases are in fact inborn errors of metabolism and can be controlled by appropriate replacement therapy. Sex-linked forms of Leber's disease are the commonest; examples are the families described by Russel,[6] Hogg,[7] Taylor and Holmes,[3] and the four pedigrees reported by Halbertsma.[9] In the fifth pedigree of Halbertsma's paper the first two generations are ordinary sex-linked recessive, while in the last two generations there is a change in dominance to simple dominance. Griscom[10] reported a dominant family with fourteen cases, always transmitted through the father, in three generations. Eight of those affected were male and six female. This type of transmission is much rarer than the preceding. Many pedigrees cannot be explained on the basis of sex-linked, dominant or recessive linkage, and are not fully understood. Gates,[11] in his book *Human Genetics*, has stated,

> "Evidently the problem of variable sex-linkage in Leber's disease will only be solved by further analysis of symptoms, age of onset and other details in many complete pedigrees. It is not yet certain whether a difference in method of inheritance is accompanied by differences in symptoms. The main genetic peculiarity, however, is evidently the variable dominance in the female."

Leber's disease is of particular interest to the neurologist because of its occasional coexistence with other neurological diseases. Both Snell[12] and Taylor[13] reported the association of Leber's disease with epilepsy, while Story's cases[14] were associated with insanity. Ferguson and Critchley[15] drew attention to the relationship between Leber's disease and heredo-familial ataxias. Their cases showed variously, epilepsy, mental defect, pyramidal disease, ataxia and areas of anæsthesias. Holmes and Taylor[8] reported 11 patients with Leber's disease accompanied by mental changes, areas of anæsthesia, and absent knee and ankle jerks. The optic atrophy sometimes encountered in Friedreich's ataxia and in Marie's cerebellar ataxia may well be related to Leber's optic atrophy. Merritt[16] described pes cavus resembling that of Friedreich's ataxia in one of his cases of hereditary optic atrophy.

Pathological reports are scanty. Rehsteiner[17] described the changes in a case examined seven years after onset. He found atrophy of the ganglion cells, especially near the macula, and degeneration of the nerve fibre layer in the retina. The papillomacular fibres in the optic nerves were demyelinated and surrounded by an increase in glial fibres. Other parts of the optic nerves were normal. There was no inflammatory process and he interpreted the changes as being evidence of primary degeneration. Fisher[18] suggested that the optic atrophy is secondary to swelling of the pituitary, and Kuhn[19] decompressed the optic

nerves in a case of Leber's disease. At operation no evidence of pituitary enlargement was noted, nor did the procedure have any effect on the condition. X-rays of the skull have repeatedly failed to demonstrate enlargement of the sella turcica; no endocrine disturbance has been noted, and the type of visual field loss, *viz.*, central scotoma, is against any lesion originating in the pituitary. Raaf and Baer[20] have reported four cases in which the scotomata were bitemporal, and in these cases x-ray failed to demonstrate any enlargement of the pituitary fossa.

Our interest in this condition stemmed from examination of the first patient illustrated in Table I. Complete examination, including serology and cerebrospinal fluid, revealed no abnormality save for the visual disturbance.

In view of the family history of visual failure a diagnosis of Leber's hereditary optic atrophy was made, and it was decided to investigate those members of the family who were available. No less than 13 relatives of our patient were located and examined and found to have optic atrophy. Details of the family's pedigree were obtained to date and are graphically shown in Fig. 1. The pedigree is complete to the sixth generation and covers 670 persons. The majority of the family is located in Eastview, Ont., a small town near Ottawa. The investigation was carried out in the homes of the individuals by one of us (A.V.B.) assisted by two social service workers, the one acting as secretary, the other establishing liaison with the various families. This worker was especially suited to the job as she was of French extraction and had formerly worked near Eastview. She saved much time for the physician by locating the patients in advance and removing from them any apprehension by explaining the purpose of the examination without awakening any unjustified hopes. Examination of the nervous system and the optic fundi was made, together with as good an estimation of the visual fields as could be carried out in the individuals' homes. A summary of the findings is listed in Table I.

DISCUSSION

In this series of cases it will be noted that the age of onset varied from 10 to 48 years, and that the average age of onset was 29 years—six years older than the age quoted by Bell.

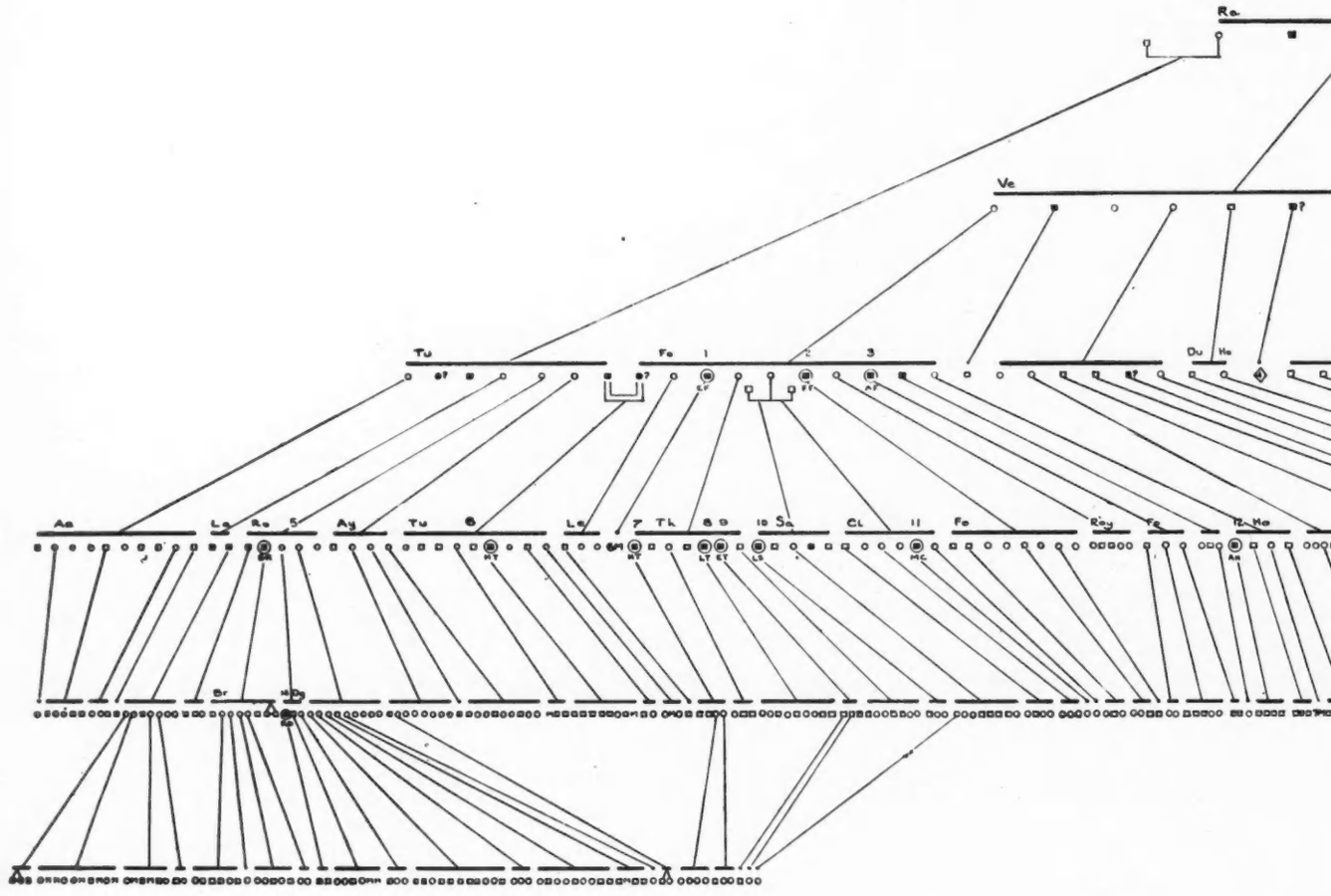
Eleven patients showed some improvement of vision at periods varying from 6 months to 3 years after the onset. Two stated that visual failure had progressed up to a point and then become static with no tendency towards remission. Case 1 was seen too soon after onset for any improvement to have started. Tendency towards improvement was independent of age of onset.

No females with the affliction were seen, but the four marked in the pedigree, of the third generation, were known to have "very bad eyes", which the family considered to be similar to the trouble of the male members. It is noteworthy that two of these females in the family "Ro" were mentally backward and inmates of a mental institution, as was their brother who had optic atrophy. Others in the pedigree in mental institutions were the fourth brother of Cases 2, 3 and 4, and a sister of Case 1.

The pedigree shows two marriages between cousins, the first in the second generation leading to the two daughters and one son ending up in a mental hospital, as mentioned above. The subsequent issue of this line surprisingly enough does not show any unusual degree of abnormality. The second marriage between cousins occurred in the third generation and led to case 1 above, whose sister was mentally retarded. The grandchildren of this union are all under 10 years and may well develop optic atrophy or other abnormalities as they grow older. In fact, the majority of the members of the fifth and sixth generations have still to approach, or are within, the age-period of onset, and may yet develop optic atrophy.

The method of transmission seems to be a gynephoric sex-linked recessive, as is borne out by the great paucity of affected females (3 questionable cases as compared to 32 males), and the surprisingly close approximation of the number of those actually affected to the expected number, on a sex-linked basis. The data are in close accord with the hypothesis of sex-linked recessive inheritance in view of the segregation in the sibships containing at least one affected member. All these families were related to the main pedigree through the *mother*, who should therefore be heterozygous (if the hypothesis is true). If the father is unrelated, the expectation in such crosses is therefore one affected male, one normal male and

LEBER'S
PEDIGI



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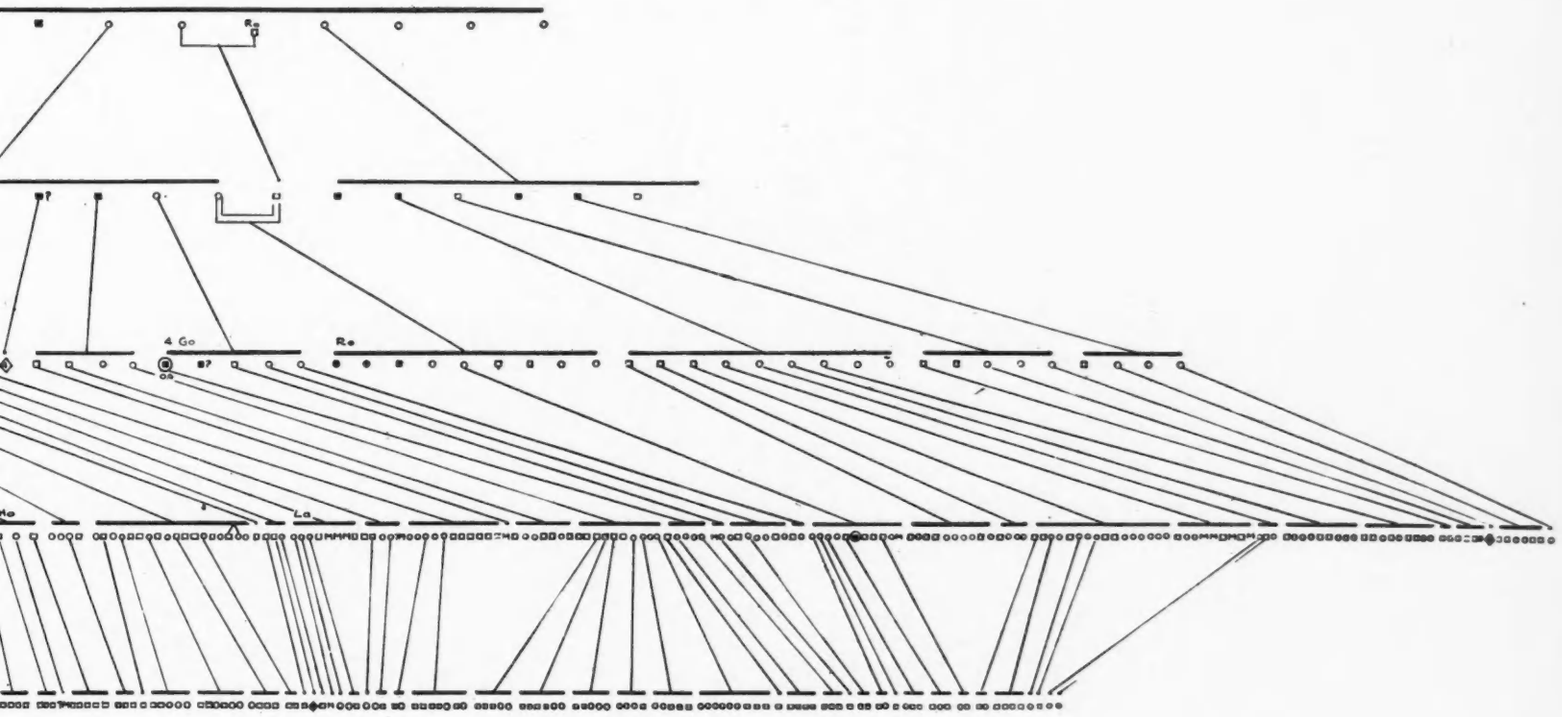
PEDIGREE OF A CANADIAN FAMILY



LEGEND

□ MALE	◈ 4 OFFSPRING, SEX UNKNOWN
○ FEMALE	◈ SEX UNKNOWN, NUMBER UNKNOWN
■ AFFECTED MALE	M MISCARRIAGE
◉ AFFECTED MALE EXAMINED	IDENTICAL TWINS
■? POSSIBLY AFFECTED MALE	NON-IDENTICAL TWINS
● AFFECTED FEMALE	COUSIN MARRIAGES
●? POSSIBLY AFFECTED FEMALE	

TABLE I.

SUMMARY OF CASES EXAMINED

Case	Age at exam.	Age at onset	Visual acuity Right	Visual acuity Left	Scotoma	Optic discs	Rate of onset	Mode of onset	Maximum visual loss	Degree of recovery
1	33	33	Fingers at 2 feet		Central, bilat.; peripheral isopters reduced.	White	5 months	Both eyes		Too recent for recovery
2	63	±40	20/50	20/50	Paracentral, bilat.	Mod. pale	Sev. months	Both eyes	?	Some improvement by one year; stationary since
3	54	15	20/50	20/50	Central, bilat.; large		Rapid, sev. days gradual, 12 mos.	L. first R. after 3 mos.	Light only	From awareness of light to reading large print, over 6 months
4	56	48	20/50	20/50	Central, bilat.; small	White	Gradual, 4 weeks	Both eyes	Incapacitating	Improvement over several months
5	60	30	Light only		Central, bilat.; large	White	Overnight	Both eyes	Incapacitating	None
6	56	40	20/70	20/200	L.—central, large; R.—paracentral, small	L.—pale R.—less marked	Sev. days	L. first R. after 6 mos.	Incapacitating	Some improvement after several months
7	52	47	20/50	20/50	Paracentral, bilat., small; enlarg. blind spots	Pale	Sev. weeks	Both eyes	Not incapacitating	Slight
8	43	10	20/100	20/100	Central, bilat.; small	White	Sev. months	Both eyes	Incapacitating	Static for 6 months, then some improvement
9	38	27	20/50	20/50	Central, bilat.; small	Pale, marked in R.	Rapid, few days, gradual, 3 mos.	Both eyes		Slight improvement
10	33	16	20/20	20/20	Paracentral, bilat.; small	White	Rapid, few days, gradual, 1 month	L. first R. after few days	Light only	Static for 6 months, then marked improvement
11	38	21	20/40	20/100	L.—central, large; R.—paracentral, small	White	Overnight	Both eyes	Could not read	*Static for 3 years, then some improvement
12	27	24	20/70	20/70	Paracentral, bilat.; small	Mod. pale	Few days	Both eyes	Almost blind	Static for 18 months, then some improvement
13	25	20	20/40	20/40	None. Bilat. enlarg. of blind spots	Pale	12 months	Both eyes	Not incapacitating	None
14	33	27	R. and L. less than 20/200		Too blind to test	White	Overnight	Both eyes	Incapacitating	Static for one year, then some improvement

*This is a surprisingly late remission, but the patient was sure that it was three years before he noticed any return of vision.

two normal females. That this is true is borne out by the following table, which excludes the offspring of consanguineous marriages:

	Males		*Females*	
	Affected	*Normal*	*Affected*	*Normal*
Expected	27	27	0	54
Observed	29	27	0	51

No other mode of inheritance could reasonably give this pattern.

The only deviation from expectation is the consanguineous mating, in the second generation, that produced two affected females from normal parents. To account for this one would have to postulate either (*a*) that the gene sometimes expresses itself in heterozygous females (as Gates[11] has reported), or (*b*) that the gene occasionally fails to express itself in hemizygous males — the phenomenon of "reduced penetrance" often observed in human genetics.

The fact that in no case is there evidence that an affected male transmitted the condition to his grandson may suggest that this is more than a sex-linked recessive. One might almost consider sex-limited transmission, but the presence of possibly affected females and some 40 normal sons produced by affected fathers rules this out. If this were indeed a sex-limited condition, the possibility of the use of œstrogens therapeutically or prophylactically suggests itself.

In speculating as to the etiology of this condition a comparison with subacute combined degeneration of the spinal cord suggests itself. It is possible that there is an optic neurotrophic factor essential for the well-being of the optic nerve resembling the neurotrophic factor necessary to keep the posterior and lateral columns of the spinal cord healthy. Like this substance, the optic nerve factors may be dependent on extrinsic and intrinsic principles. In Leber's disease, owing to an abnormality of some of the genes, there may be a deficiency of an enzyme necessary to liberate the intrinsic optic nerve factor. Optic atrophy may result when this latter substance becomes deficient, or from deficiency of extrinsic factor aggravated by insufficient supply of intrinsic factor. Therapy with liver has so far not proved effective.

An alternative possibility is that, due to an abiotrophy, the optic nerve is unusually vulnerable, so that insults which would be well tolerated in the normal, cause the vulnerable optic nerve to atrophy. Cases 1, 7 and 14 had their onset associated with periods of excessive indulgence in alcohol. Many people drink just as heavily as these three individuals without suffering optic atrophy. If the alcohol was a precipitating factor it may have been because these individuals had abnormally vulnerable optic nerves.

Bell and O'Neill[1] have given an excellent description of the optic atrophy which occurred in 115 Canadian soldiers captured by the Japanese at Hong Kong in 1941. They comprised 20% of the returning force of 560 men. The mode of onset and findings were in some instances similar to those of hereditary optic atrophy, but they occurred under conditions of caloric and protein deficiency, lack of B-complex factors and ingestion of spoiled, polished rice. Later treatment with thiamine and B-complex was ineffective. This might be a lead, however, for the trial of prophylactic treatment in families with hereditary optic atrophy.

SUMMARY

A Canadian family with hereditary optic atrophy is described. Fourteen affected patients were examined, and the pedigree was constructed to six generations, involving to date 36 affected persons out of a total of 670 in the pedigree. Many of the young are potential future victims. The condition is probably a genetic fault involving essential enzyme systems. Clinically it resembles the optic atrophy which developed in mal-nourished Canadian prisoners held captive by the Japanese in World War II. A large prophylactic, nutritional experiment seems to be indicated with a family subject to Leber's hereditary optic atrophy.

We are pleased to acknowledge the great help rendered by the Social Service Department of the Montreal Neurological Institute, notably Miss Gabrielle Bourque and Mrs. E. McL. Davidson, in locating these families, and their part in collecting the data for the pedigree.

We are also grateful for the assistance and advice of Dr. F. Clark Fraser and Dr. J. W. Boyes, of the Department of Genetics, McGill University, in assessing the pedigree.

REFERENCES

1. BELL, P. G. AND O'NEILL, J. C.: *Canad. M. A. J.*, **56**: 475, 1947.
2. DENNY-BROWN, D.: *Medicine*, **26**: 41, 1947.
3. BELL, J.: The Treasury of Human Inheritance. Hereditary Optic Atrophy, Vol. 2, Cambridge University Press, 1931.
4. VON GRAEF, A.: *Arch. f. Ophth.*, **4**: 266, 1858.
5. LEBER, T.: *Arch. f. Ophth.*, **17**: 249, 1871.
6. RUSSEL, W. R.: *Tr. Ophth. Soc. U. Kingdom*, **51**: 187, 1931.
7. HOGG, G. H.: *Med. J. Australia*, **1**: 372, 1928.
8. TAYLOR, J. AND HOLMES, G. M.: *Tr. Ophth. Soc. U. Kingdom*, **33**: 95, 1913.

9. HALBERTSMA, J.: *Nederl. tijdschr. v. geneesk*, 78: 1705, 1934.
10. GRISCOM, J. M.: *Am. J. Ophth.*, 4: 347, 1921.
11. GATES, R. R.: Human Genetics, Macmillan, New York, 1946.
12. SNELL, S.: *Tr. Ophth. Soc. U. Kingdom*, 17: 66, 1896-97.
13. TAYLOR, S. J.: *Tr. Ophth. Soc. U. Kingdom*, 12: 146, 1891-92.
14. STORY, W.: *Ophth. Rev.*, 4: 33, 1885.
15. FERGUSON, F. R. AND CRITCHLEY, M.: *J. Neurol. & Psychiat.*, 9: 120, 1928.
16. MERRITT, H. H.: *Arch. Neurol. & Psychiat.*, 24: 775, 1930.
17. REHSTEINER, K.: *Arch. f. Ophth.*, 125: 14, 1930; Abst. *Brit. J. Ophth.*, 16: 241, 1932.
18. FISHER, J. H.: *Tr. Ophth. Soc. U. Kingdom*, 36: 298, 1916.
19. KUHN, H. S.: *Arch. Ophth.*, 5: 408, 1931.
20. RAAF, J. E. AND BAER, H. L.: *Am. J. Ophth.*, 21: 384, 1938.

RELATIONSHIP BETWEEN GOVERNMENT MEDICAL SERVICES AND THE CANADIAN MEDICAL PROFESSION*

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THE Program Committee of our Association in asking me to speak at the General Session of this Eightieth Annual Meeting of the Canadian Medical Association had in mind, I presume, that a brief outline of the policies used in building up the Treatment Services of the Department of Veterans' Affairs would be presented. In addition to doing this, I propose to touch on the relationship and effect of this Federal treatment organization on the Canadian medical profession as a whole.

A. *Immediate emergency reorganization.*—With the cessation of hostilities of World War II in the spring of 1945, the Treatment Services of the Department of Veterans' Affairs were reorganized. This reorganization was made on long term planning but its immediate objective was to give medical care for the tremendous number of Canadians who were being demobilized. In this period of demobilization, it was necessary to procure rapidly for the Department additional hospital beds and personnel to care for the wounded or sick veteran who was placed in these beds.

In addition to the hospitalization program necessary, there was a great deal of out-patient work to be done. Two fundamental principles were established to meet this emergency of a tremendous increase in the patient load of the Department. The first was that the machinery was established for the employment of part-time physicians, both general practitioners and specialists. This employment could take place rapidly without the cumbersome and, at that time, lengthy procedure of Civil Service appointments. The second principle that was established was that the veteran entitled to treatment, apart from those who were hospitalized in Departmental hospitals, should be allowed to have his doctor of choice. In other words, the veteran was allowed to go to whichever doctor he desired rather than to any appointed representative of the Department. The medical profession of Canada responded, as one would expect, and we were able to obtain on a part-time basis the best specialists in the country to treat veterans in our own institutions. The great volume of work done outside our institutions was carried out in a most satisfactory manner by the medical profession of Canada who were not Departmental employees but who worked on a schedule of fees basis.

One other principle that was adopted to meet the emergency of demobilization was the utilization wherever possible of Active Service hospitals which were no longer needed by the Armed Services. Some 22 of these hospitals were taken over; only 5 are still operated by the Department. Thus, a hospital building program was avoided for a peak load of patients at a time when construction of any kind was very difficult.

So much for the policies that were initiated to meet the emergency of increased medical care needed for the demobilizing Armed Services. They were the rapid employment of many part-time doctors, the utilization as far as possible of the practising physicians of the country on a schedule of fees basis, and, lastly, the utilization of existing Service hospitals until the peak load of hospitalization was over.

B. *Long term policies.*—With the reorganization of the Treatment Services of the Department in 1945, certain policies were adopted which we believe have proved themselves as essential in the building up of excellent medical treatment for the veteran.

1. *University affiliation—teaching hospitals.*—Where either postgraduate or undergraduate teaching is being done in a hospital, it is a

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great incentive to good Medicine. With this in mind, the various medical schools across Canada were contacted and an affiliation established between Departmental hospitals and the various Faculties of Medicine.

This affiliation and co-operation between universities and the Department has been of great mutual advantage to both parties and has been the greatest single factor in making it possible for the Department to provide the highest type of medical care for the veteran. Teaching has been chiefly postgraduate but a great deal of undergraduate teaching is taking place in many of our hospitals. The departmental hospitals have helped and are helping to provide much needed facilities for postgraduate instruction in Canada. In many localities where the teaching material in civilian teaching hospitals has declined markedly due to various factors departmental hospitals have provided facilities for a very considerable amount of undergraduate teaching.

2. *Part-time specialists and interns.* — It is obvious that these hospitals could more readily become real teaching hospitals if the members of their staffs were also members of the Faculties of Medicine of the associated universities. As pointed out above, we were able to hire part-time specialists without reference to civil service regulations. These were hired rapidly and were for the most part members of the Faculty of Medicine of the university in the district where the veterans' hospital was situated. These part-time specialists are the mainspring of the treatment services. They represent, I believe, the finest in Canadian medicine. They usually teach part-time in a civilian teaching hospital and carry on a limited consulting practice. While those specialists who were demobilized from the Services found their employment with the Department a very desirable rehabilitation measure to get them reestablished in their special practice, they have, by and large, continued to serve the Department and now in 9 cases out of 10 at a financial loss to themselves.

Having established then this class of staff man of very high calibre, it is obvious that one must have a great deal of the work in a hospital done either by interns or full-time general duty medical officers. Our policy is very definite that this work shall be done by interns who come to the Department for a year or two for postgraduate work and then proceed elsewhere for further training. With certain exceptions such as radiologists, anæsthetists, laboratory directors, we believe doctors having to do with the diagnosis and treatment of the sick veteran should not be full-time general duty civil service employees. We therefore have a professional staff made up of a very minimum number of full-time state employed doctors.

3. *Professional advisers to the department.*— The head office staff of the Treatment Services of the Department of Veterans' Affairs at Ottawa is purely an administrative staff. Professional advice is constantly sought by it and furnished by designated specialists in various fields who are actually practising their specialty in universities and in our hospitals. This is stressed because professional policy is largely determined by these advisers and this professional policy reflects the best medical thinking and does not represent a head office Government dictated policy. This, I believe, is most important; how medicine should be practised can best be determined by the highest skilled specialists whose integrity and professional skill reflects the best in Canadian medicine. I stress again that this advice comes not from full-time Government employees but from the best of our university staffs and profession generally in Canada.

Another safeguard in securing advice on policy at a sane, sound but yet progressive level from the doctor in consulting practice or in a high academic post is the medical advisory committee to the department. This committee is composed of outstanding medical men from the various universities across Canada who are employed with the department to a very slight extent, or not at all. This medical advisory committee then is one largely of non-departmental employees. It is available for consultation at any time and meets annually in Ottawa at the time of the meeting of the Royal College of Physicians and Surgeons of Canada. Again, this step has been taken to have further advice on policy from non-departmental doctors who are outstanding leaders in their specialties across Canada.

4. *Medical advisory boards.*—In order to obtain the greatest efficiency in each of our D.V.A. hospitals, medical advisory boards have been set up. These boards consist of the heads or directors of the services and correspond to

medical advisory boards in civilian teaching hospitals. The advice of these boards carries great weight in what goes on in the hospital and also regarding any general policy. This again is a means of making advice on policy and local arrangements the responsibility of local medical authorities in the D.V.A. hospital. Though the final administrative authority must emanate from head office, this administrative authority is not autocratic and advice from the various sources mentioned above determines administrative action unless there is very good reason to the contrary.

What we have tried to do is to have head office run the medical service on the advice of the most competent practising and teaching physicians in the country.

C. *Relationship with the Canadian medical profession.* — The above measures, adopted to meet the demobilizing emergency and particularly the above policies adopted as long term policies of the department, have and are having considerable effect on the general medical profession. I will enumerate a few of these.

1. *Providing postgraduate study.*—(*a*) For the general practitioner, certain D.V.A. hospitals which are not in close proximity to university centres provide excellent training in general medicine and surgery for a doctor going into general practice. In these hospitals the rare and more complicated work done in university teaching hospitals is not undertaken and the graduate receives training particularly suited to his taking up general practice. Also, as many of you are aware, refresher courses for general practitioners have been and are being put on in D.V.A. hospitals and apparently are appreciated by the general practitioners attending them. (*b*) For the specialists. Specialists' training is provided in practically all D.V.A. hospitals. These hospitals have been approved by the Royal College of Physicians and Surgeons of Canada for training in designated specialties in each hospital. The postgraduate student avails himself of these facilities in either of two ways. The first is that his time spent in a D.V.A. hospital in a specialty is part of an organized postgraduate course, that is, for a part of his five years' postgraduate work the university designates that he should go to a D.V.A. hospital for so much of that time. Secondly, certain students obtain postgraduate work towards their Certification or Fellowship by the Royal College in D.V.A. hospitals apart from any organized course put on by the university. These postgraduate facilities are much needed in Canada.

2. *Doctor of choice plan.*—This plan giving free choice of doctor to veterans who reside where there is no D.V.A. hospital is considered advantageous both to the veteran and to the medical profession. The work of the Doctor of Choice Plan was facilitated greatly by the Canadian Medical Association setting up local Advisory Committees in the various D.V.A. districts to advise the local Department administration regarding the functioning of this plan.

The initial step in setting up the Doctor of Choice Plan in consultation with the Canadian Medical Association was the establishing of a schedule of fees that the Government would pay to doctors for services rendered to the veteran. This schedule of fees as drawn up by your Association entailed a tremendous amount of work. I believe that to have such a schedule of fees, generally deemed adequate, applicable across Canada has been to the distinct advantage of the Canadian medical profession.

3. *Classes of veterans treated by the Department of Veterans' Affairs.*—The prime function of the Treatment Services of the Department of Veterans' Affairs is, of course, the medical care of the pensioner. The pensioner is provided this treatment by right. In other words, he is entitled to it by Act of Parliament.

There is another class of veteran who is treated when facilities are available in departmental hospitals. These are veterans with meritorious service who by a means test applied by the department are not considered to have sufficient funds to provide their own treatment privately.

As many of you are aware, the department is presently in the process of initiating a scheme whereby veterans may insure themselves by a special prepaid medical insurance plan. If and when this plan is initiated—we hope through existing insuring plans—the veteran if he so chooses may be treated in a veterans' hospital. His dependents will be treated by the civilian medical facilities available and not in departmental hospitals. In other words, an attempt is being made to have a large volume of veterans take out prepaid medical insurance voluntarily. When this scheme is in force, I believe it will be

a distinct aid to what appears to be the present solution to the general medical treatment problem in Canada. This problem seems to me to be very simply that medical science has made so much progress in the last few years and that progress has resulted in an ever increasing cost to the patient so that it has become next to impossible for a large proportion of the general population of Canada to pay for a severe illness of any duration. When the benefits of good treatment are kept away from any sizeable group in the community, there is bound to be and I think should be some change in the medical set-up to make it possible for this group to obtain these advantages. Because we think it is to the advantage of the veteran and of medicine generally in Canada that as many people as possible take out prepaid medical coverage this plan is being initiated. If some such plan as this is not initiated, it is my feeling that other schemes not as advantageous to the medical treatment of the veteran or to the medical profession may be initiated.

4. *Special services.* — (*a*) *Paraplegics.* Because the Department of Veterans' Affairs is committed to treat certain types of war injuries it is obvious that if these war injuries are looked after properly, certain special treatment centres will be created for this purpose. An example of this are the paraplegics, of which there were some 200 in World War II. In order to treat these unfortunate veterans very special treatment facilities and rehabilitation measures had to be provided. The provision of paraplegic centres for the treatment of veterans only, will be considered as the first step in providing adequate treatment for all parapelgics, civilian as well as veteran. As a result of the adequate provision of these facilities, some 80% of the veteran paraplegics are now rehabilitated into civilian life. There were not available to civilian paraplegics such facilities in Canada when the department initiated its program or if they were available, they were available to a very minor degree. Since the paraplegic, although he has been rehabilitated and is back in civilian life, tends to have relapses such as kidney infections, etc., which necessitates immediate highly skilled treatment, it is felt that some of these centres at least should be kept on and even though the bulk of the veterans have been discharged facilities should be readily available should they become ill again.

In order to keep highly trained staff in these centres with a dwindling number of patients, it was decided that civilian paraplegic patients could be admitted, provided there were no adequate treatment facilities in the civilian hospitals and provided some body reimbursed the Federal Government for their care. This is the second step where the department is running a paraplegic centre treating both veterans and civilians, this, because there are not adequate civilian facilities available.

The third step has already taken place in British Columbia and will shortly take place in Ontario and Quebec, and consists of local organizations setting up and operating paraplegic treatment centres for the treatment of civilian paraplegics and the veteran paraplegic if he needs care. The department will thus cease to have paraplegic centres. It would appear obvious from the above that the Treatment Services, by establishing adequate treatment facilities for veteran paraplegics, have markedly hastened the establishment by non-Governmental organizations of this service for the general civilian population.

(*b*) *Severe poliomyelitis.*—Many of the patients suffering from severe poliomyelitis may have residual paralysis demanding the specialized treatment given to the paraplegic. It was stated by competent medical authorities that in many places there were not civilian rehabilitation and retraining physical medicine facilities adequate to look after this group, the poliomyelitis cases with a very severe residual disability. Since these cases required the same type of training as the paraplegic, severely handicapped civilian poliomyelitis cases were admitted to D.V.A. paraplegic centres for treatment.

(*c*) *Deforming arthritis.*—It became obvious during the war that one of the big problems that would face the Department of Veterans' Affairs would be the treatment of veterans suffering from crippling arthritis chiefly rheumatoid arthritis. Special arthritic clinics were set up in D.V.A. hospitals across Canada. In these clinics, all known available methods of diagnosis and treatment were applied. The results were much more gratifying than was even hoped for.

It was found that in certain cases of crippling arthritis after an accurate diagnosis had been made and any special forms of therapy

undertaken that there was a group which required prolonged stay in hospital under constant supervision. By departmental regulations, it was possible to give these veterans this prolonged treatment and the resulting percentage of cures or marked improvement was very high. One might compare this type of treatment for arthritics to the sanatorium care for the tuberculous. With the shortage of active treatment beds in the country, there are very few places where facilities are available for this type of care. However, the demonstration of the good results obtained in D.V.A. hospitals has led to the establishment of such facilities in certain civilian hospitals across the country. Pending the establishment of these facilities in civilian hospitals, the Department has considered the advisability of admitting a limited number of suitable civilian cases to Departmental Arthritic Clinics. Up to date this has not been done. It is hoped that civilian facilities will become adequate so that the Department will be responsible only for the veteran arthritic. There are more than enough of these to tax our present facilities.

(*d*) *Geriatrics.*—The department is committed to the care of the ageing veteran who for physical reasons is not able to care for himself. This increasing problem has again necessitated the creation of special centres and institutions for the care of the ageing. It has been found possible to do a great deal to improve the health, happiness and usefulness of many of this class of patient. Special studies are going on in the department regarding the best methods of caring for them. The results of this research or investigation, we hope, will add knowledge which can be applied to the general problem of the care of the aging throughout Canada.

It will be seen from the above that due to certain war injuries such as amputations and injury resulting in paraplegia and because of certain facilities for the treatment of other conditions which the department has, which are not readily available in civilian medicine, certain special treatment centres have been built up. I believe that these have tended to improve the standards of general medical practice in Canada and they have been installed in Veterans' Affairs hospitals to look after veterans. Similar facilities are being made available and we hope will continue to be provided by other than the Federal Medicine Service for the treatment of civilians suffering from these special conditions.

The present D.V.A. hospital facilities have been taxed to the limit this past winter. It is not anticipated that there will be any appreciable falling off in the patient load; the present hospital facilities will be needed for many years to come to look after those veterans entitled to treatment. There is no intention of expanding the present departmental hospital facilities and those presently in existence will be needed for the care of the entitled veteran.

CONCLUSIONS

1. The policies adopted by the Department of Veterans' Affairs to meet the sudden rapid increase in patient load as a result of demobilization of the Armed Services have been reviewed. By the temporary utilization of the Service hospitals, the services of the practising physician on the schedule of fees basis and by the utilization of part-time doctors, both general practitioners and specialists, a temporary marked increase in the work to be done by the Department of Veterans' Affairs has been accomplished. This has been accomplished efficiently and without the setting up of a large permanent medical service.

2. Certain long term policies adopted by the department in 1945 have been reviewed. These in essence are: veterans' hospitals should be teaching hospitals closely associated and affiliated with the various faculties of medicine across Canada; the staff in these hospitals, with certain exceptions, who have to do with the diagnosis and treatment of the sick should be part-time specialists on the staff of the university or engaged to a small degree in private consulting practice. The remainder of the work in hospitals should be done by interns pursuing their postgraduate education. These interns are employed with the department for a limited period of time and then proceed elsewhere. Those doctors employed should have an outside interest or stimulus, *i.e.*, university appointment or private consulting practice, to keep the standard of medicine at its highest, or should be temporary employees such as postgraduating interns. It is the policy of the department that full-time state employed civil service doctors should be employed to a very minimum.

3. The influence of the teaching program and the method of employment of physicians has resulted in an excellent medical service being provided for the Canadian veteran. It is not

intimated that the principles employed in the creation of this medical service might be applicable to the entire population of Canada but the advantages of the employment of part-time medical men are stressed. The employment of full-time state employed medical men should be kept at a minimum. The advantages also of having the policy of any federal or state run medical service not dictated from head office are stressed. Advice on policy should be sought from those best qualified in university work and the outstanding consultants in private practice across the country.

4. In a good state-run medical service dealing with war casualties and pensioned veterans, the very nature of the work will demand the creation of certain special centres for treatment. These special centres for treatment such as those made available to the paraplegic may surpass treatment facilities for these conditions available to the civilian population. As soon as possible, civilian facilities of one kind or another, such as our special treatment centres, should be created for the treatment of these special disabilities occurring in the civilian population.

AEROSOL THERAPY IN THE TREATMENT OF POSTOPERATIVE PULMONARY ATELECTASIS*

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THERE is considerable difference of opinion whether immediate bronchoscopic aspiration or medical treatment should be instituted when postoperative pulmonary atelectasis is diagnosed. Both methods have their proponents. When medical treatment is employed a tendency exists to go directly to the use of antibiotics without much regard for bronchial obstruction and the mechanical principles involved. The postoperative patient who develops a fever is often given penicillin, or streptomycin, or both. The immediate infection is controlled, but the remote results of the obstruction which may be important are forgotten.

There are therefore two important points to remember. First, to suspect atelectasis in every postoperative case which develops fever; second, to remove the bronchial plug which is of paramount importance. It is our contention and experience that this can usually be performed more easily and comfortably for the patient by medical means than in any other way.

Previous publications[1, 2] have emphasized the principles upon which medical therapy is based. The treatment is founded on the premise that the atelectasis is due to tenacious mucus plugging the bronchus, and that generalized bronchospasm tends to hold this plug in place.

The treatment attempts to do four things: (1) Liquefy the mucous plug. (2) Release the bronchospasm. (3) Allow the liquefied plug to slip out by gravity. (4) Reinforce these by the expulsive force of cough.

These steps are accomplished by instituting the following measures: (1) Using an expectorant mixture. (We usually employ mist. ammonii chloridi). (2) Employing a bronchodilator (*e.g.*, epinephrine). (3) Posturing the patient to allow gravity to take effect. (4) Encouraging cough. Sulfonamides and antibiotics are used as indicated throughout the treatment.

Previously we have used ephedrine subcutaneously as a bronchodilator. In the past year we have employed aerosol therapy for our bronchodilation, and feel our experience is worth recording.

Material.—During this period 23 cases of postoperative pulmonary atelectasis were collected. These are summarized in Table I. They occurred on the surgical wards of the Royal Victoria Hospital. The diagnosis in all cases was made on both clinical and radiological evidence. The recognition of the complication was usually made in the first 24 to 48 hours postoperatively. The signs and symptoms of onset of atelectasis were insidious in 17 cases and sudden in 6. A rising temperature, 101 to 103°, increasing pulse rate, difficulty with expectoration, listlessness, in some cases anxiety, were almost invariably present. As a group these patients were inactive compared to the normal, actively moving postoperative patients. This was particularly true of 11 of these patients who underwent pulmonary surgery. Chest pain on breathing, coughing and moving, was a major factor here.

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The entire group varied from 14 to 70 years of age. There were 13 males and 10 females. The anæsthetic was spinal in 13 cases (10 male and 3 female), and general inhalation in 10 cases (3 male and 7 female). The patients who had a general anæsthetic were intubated with a McGill tube which had an inflatable cuff on its tracheal end. These latter patients all had an irritating cough with fairly large amounts of thick tenacious mucoid expectoration for 3 to 7 days postoperatively. The duration of the operations was from one-half to six hours. There was no correlation between pre- and post-operative sedation and the occurrence of atelectasis. Carbon dioxide rebreathing bag exercises were started routinely immediately on return to the ward in all patients who had spinal anæsthesia. There were six patients who, following their general anæsthetic, did not immediately receive the carbon dioxide rebreathing bag exercises, but got them later.

Treatment and results.—The treatment in every case following the recognition of the atelectasis was: (1) Heavy doses of expectorants, such as mist. ammonii chloridi or mist. pectoralis, drachms 4 every 4 hours. (2) Aerosol therapy. (3) Increased general prophylactic measures, *e.g.*, frequent movement and posturing of the patient; encouragement to cough and expectorate; and breathing exercises every waking hour, if not already being done, with the rebreathing bag containing 95% oxygen and 5% carbon dioxide. (4) Antibiotics, either parenterally or via aerosol, or both.

Aerosol was administered in 1 c.c. amounts every 2 to 3 hours 5 to 8 times a day. A suitable nebulizer of the deVilbiss No. 40 or vaponephrine type was used. The pressure source for the nebulizer was an oxygen cylinder with a suitable reducing valve and flow meter attached. The insertion of a Y-tube at a convenient place in the rubber tubing near the nebulizer enabled the patient to operate the production of aerosol at will. The aerosol solution used was: epinephrine 1% and ephedrine 1% in proportion of 1:9 in 9 cases; neosynephrine 1% alone in 11 cases; and various combinations of these drugs in the remaining 3 cases (see Table I). The dose of antibiotic drug added to the aerosol depended on the gravity of the signs and symptoms and the predominating micro-organism in the sputum. Penicillin 20,000 to 50,000 units, streptomycin 50,000 to 200,000 units, or both, were not infrequently dissolved in the aerosol solution.

The treatment was supplemented with bronchoscopic aspiration in 5 patients, 2 of whom required a second aspiration.

Excellent results were obtained in 17 cases, with complete clinical and radiological recovery in 1 to 7 days. In 10 cases re-expansion of the affected lobe had occurred in less than 4 days. Fair results were obtained in 4 cases, with complete clinical recovery in 11 to 17 days, and radiological clearing in 11 to 21 days. In 2 cases the results were poor, with eventual re-expansion in 12 weeks. Both of these cases had bilateral bronchiectasis.

The following are representative case histories.

CASE 8

D.C., aged 24, female. Admitted to Royal Victoria Hospital with intestinal obstruction, having had an appendectomy some 5 years before. The admission chest x-ray was normal. Under spinal anæsthesia, the obstruction was relieved by severing adhesive bands in the abdomen. She received the routine prophylactic breathing exercises into the CO_2 rebreathing bag. On the first postoperative day she was quite listless and made little attempt to be active. She developed a low grade fever, increasing to 103° on the second postoperative day, plus a continuous slight hacking cough with little expectoration. Chest examination revealed bilateral râles over the lung bases and one patch of blowing breathing at the left base. A chest x-ray revealed bilateral lesions radiating out from the hilar regions (see Fig. 1A). Treatment consisted of increased activity; encouragement to cough and expectorate; posture; breathing exercises with the CO_2 bag; mist ammon. chlor. drachms 4 every 4 hours; and aerosol therapy using 1 c.c. of 1% neosynephrine with 30,000 units of penicillin in the aerosol solution every 2 hours 6 times a day. Chest signs, temperature and pulse returned to normal in 24 hours, and a chest x-ray showed almost complete clearing in 48 hours (Fig. 1B). A later film 7 days after the diagnosis showed normal lung fields (Fig. 1C).

Comment.—Postoperative inactivity was the major contributing factor in the occurrence of the pulmonary atelectasis. Radiologically the lesion could have been either bronchopneumonia or atelectasis, but its sudden appearance and disappearance confirmed the latter diagnosis.

CASE 10

I.S., aged 70, female. Admitted to Hospital where a laparotomy revealed an inoperable carcinoma of the stomach. The operation was performed under general anæsthesia with cyclopropane and ether. An intratracheal McGill tube with an inflatable cuff on its tracheal end was used throughout the anæsthetic. Considering the patient's age, general condition, and ability to move, she was fairly active postoperatively. However, she was troubled with considerable mucus in her throat and had difficulty with expectoration. On the second postoperative day she had sudden precordial discomfort, dyspnæa, and slight cyanosis, a fever of 101°, a pulse of 150 with acute auricular fibrillation, and symptoms and signs of moderate shock. There was tracheal deviation to the right with distant breath sounds over the right chest. A chest x-ray film confirmed the diagnosis of atelectasis in the right lung (Fig. 2A). The fibrillation was treated with quinidine, but recurred in paroxysms. She was given mist. ammon. chlor. 4 drachms every 4 hours; postured frequently; encouraged

Case No.	Age and sex	Operation	Anæsthetic	Locale of atelectasis	Days post-operative diagnosis	Treatment			
						Aerosol solution	No. days given	Bronchoscopic No. days after diagnosis	
								First	Second
1	28 M.	Lobectomy L.L.L.	Spinal	L.U.L.	4	Epinephrine ephedrine penicillin streptomycin	9		
2	16 F.	Lobectomy L.L.L., L. Ling.	Cyclo (intubated)	L.U.L., R.L.L.	2	Neosynephrine	1	2	6
3	28 F.	Lobectomy L.L.L., L. Ling.	NO_2 ether (intubated)	L.U.L.	1	Ephedrine neosynephrine	5 7	1	8
4	25 M.	Lobectomy L.L.L., L. Ling.	Spinal	L.U.L.	1	Epinephrine ephedrine penicillin streptomycin	11		
5	43 M.	Lobectomy L.L.L.	NO_2 curare pentothal (intubated)	L.U.L., Ling.	1	Epinephrine ephedrine penicillin streptomycin	15		
6	40 F.	Thoracotomy right	Cyclo + ether (intubated)	R.L.L.	1	Epinephrine ephedrine penicillin	12		
7	20 F.	Excision of cyst., left lung	Cyclo + ether (intubated)	R.U.L.	1	Neosynephrine	8		
8	24 F.	Laparotomy freeing of abd. adhesions	Spinal	Patchy L.L.L., R.L.L.	1	Neosynephrine penicillin	5		
9	50 F.	Radical right mastectomy	Cyclo (intubated)	L.L.L.	2	Epinephrine ephedrine penicillin	4		
10	70 F.	Laparotomy ca. of stomach	Cyclo + ether (intubated)	L.L.L.	2	Neosynephrine penicillin	1		
11	52 M.	Repair of ventral hernia	Spinal	L.L.L.	2	Epinephrine ephedrine penicillin	5		
12	48 M.	Spinal fusion	Spinal	R.L.L.	2	Epinephrine ephedrine penicillin	4		
13	19 M.	Appendectomy	Spinal	R.L.L.	1	Epinephrine ephedrine penicillin	6		
14	26 M.	Closure of gastrostomy	Spinal	Patchy R.L.L., L.L.L.	2	Neosynephrine penicillin	6		
15	52 M.	Closure of traumatic bowel perforation	Spinal	L.L.L.	7	Neosynephrine	14		
16	21 M.	Repair left inguinal hernia	Spinal	L.L.L.	1	Epinephrine ephedrine penicillin	5		
17	39 M.	Trans-thoracic vagotomy left	Cyclo + ether (intubated)	R.M.L., R.L.L.	1	Ephedrine penicillin streptomycin	7	4 hours	
18	47 M.	Thyroidectomy	Avertin + ether (intubated)	L.L.L.	1	Neosynephrine	4		
19	42 F.	Laparotomy freeing of adhesions	Spinal	L.L.L.	2	Neosynephrine	14		
20	49 F.	Thyroidectomy	Avertin + ether (intubated)	R.L.L.	4	Epinephrine neosynephrine penicillin	6		
21	14 M.	Lobectomy R.M.L., R.L.L.	Spinal	R.U.L.	5	Neosynephrine penicillin	7		
22	48 F.	Lobectomy L.L.L., L. Ling.	Spinal	L.U.L.	2	Neosynephrine penicillin	15	11th day	
23	49 M.	Lobectomy L.L.L., stump. L. Ling.	Spinal	L.U.L.	1	Neosynephrine penicillin	17	6	

Recovery in days					
Clinical		*X-ray*			
Early signs	*Complete*	*Early signs*	*Complete*	*Comments*	*Results*
2	5	—	7	Following encouragement to cough with posture and aerosol, did well.	Good
4	12 weeks	7	12 weeks	Delayed expansion probably due to poor co-operation from patient to posture and expectorate. Had bilateral bronchiectasis.	Poor
8	11	9	11	Following bronchoscopic on 8th day, and intensified efforts to promote cough with posture, did well. Had bilateral bronchiectasis.	Fair
1	2	1	2	Recovery very dramatic following aerosol, posture, and encouragement to expectorate.	Good
1	12 weeks	3	12 weeks	Some pleural fluid remained and delayed expansion. Later developed a broncho-pleural fistula from which he fully recovered with good expansion. Had bilateral bronchiectasis.	Poor
3	4	—	4	Had some difficulty with chest pain and dyspnœa. Encouragement to cough with posture was rewarding.	Good
1	1	1	1	Re-expanded rapidly.	Good
1	2	—	2	Rapid recovery.	Good
2	3	—	3	Rapid recovery.	Good
2	7	2	7	Sudden atelectasis with dyspnoea and some shock plus auricular fibrillation. Symptoms all cleared including fibrillation on 2nd day.	Good
1	2	—	5	Following aerosol was able to expectorate some thick tenacious sputum with rapid recovery.	Good
1	1	—	3	Following aerosol, posturing, and coughing, did well.	Good
1	5	3	6	Following increased activity, did well.	Good
1	3	—	6	Did well.	Good
2	14	2	21	Patient not very co-operative. Prophylaxis and therapy not energetic. Had chronic cough for one year.	Fair
1	3	2	2	Rapid recovery.	Good
1	5	1	5	Bronchoscoped immediately with relief of acute symptoms. Patchy atelectasis remained which cleared in 5 days.	Good
1	3	—	3	On return from operating room was dyspnœic and cyanosed, with considerable mucus. With posture, aerosol, and encouragement to cough, recovered rapidly.	Good
1	5	—	5	On return from operating room had considerable mucus in throat. Did well with aerosol, posture, expectorants, etc.	Good
1	4	—	4	Re-expanded rapidly.	Good
1	1	1	1	Following posture and encouragement to cough recovery was dramatic.	Good
11	15	11	21	Considerable chest pain. Patient would not cough to bring up sputum. Recovered rapidly following bronchoscopy.	Fair
13	17	12	17	Inadequate nursing care and instruction in early days postoperatively. Bronchoscopic did not afford much relief. More active treatment with posture and aerosol resulted in rapid re-expansion. Difficult operation due to adhesions.	Fair

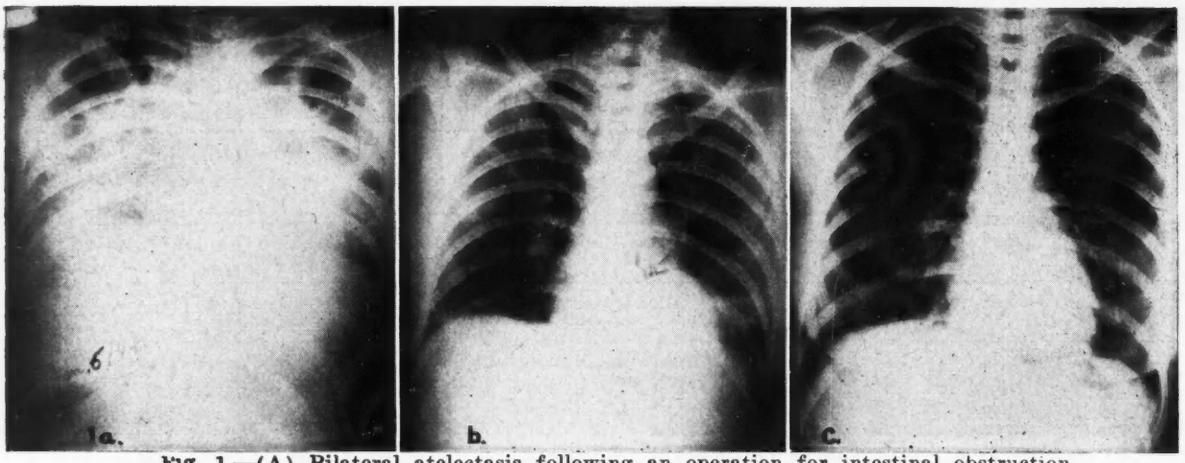

Fig. 1.—(A) Bilateral atelectasis following an operation for intestinal obstruction. (B) A chest x-ray of the same patient 24 hours after treatment was instituted. (C) The same patient one week later.

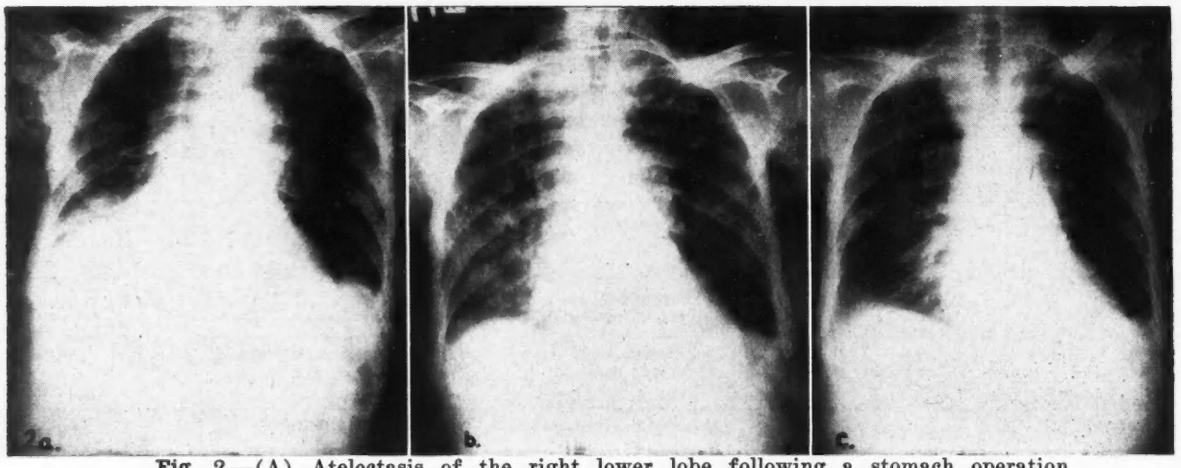

Fig. 2.—(A) Atelectasis of the right lower lobe following a stomach operation. (B) A chest x-ray of the same patient 48 hours after treatment was instituted. (C) The same patient five days later.

to cough and expectorate; and breathing exercises with the CO_2 rebreathing bag. Aerosol therapy consisted of 1 c.c. of 1% neosynephrine and 30,000 units of penicillin in the aerosol solution every 2 hours for 6 doses. By this tims she had recovered from shock with restored blood pressure, and was comfortable. When she vomited some blood the aerosol therapy was discontinued, but the remainder of the therapy was kept up. She responded dramatically, and there was considerable clinical and radiological improvement in 48 hours (Fig. 2B). She had recovered from her atelectasis 5 days later, (Fig. 2C), and there were no recurrences of her fibrillation from the 2nd day of therapy on.

Comment. — The acute atelectasis was relieved dramatically with treatment as outlined above. The signs and symptoms plus the acute auricular fibrillation represented a delicate problem in medical diagnosis and management.

CASE 13

S.B., aged 19, male. Admitted to Hospital with a diagnosis of acute appendicitis. He also complained of a chronic cough of one year's duration, but no recent upper respiratory infections. Under spinal anæsthesia an appendectomy was performed. He received the routine spinal care and the CO_2 rebreathing bag. Within 24 hours his temperature had risen to 101°. On questioning he admitted there seemed to be some phlegm in the throat which had gone into the chest. Due to fever and lassitude he was not particularly active postoperatively and furthermore there was difficulty raising his sputum due to the abdominal operation wound pain. Physical examination revealed absent breath sounds over the right base. Just above this, moderately coarse râles, occasional rhonchi and blowing breathing were heard. The x-ray film of the chest revealed an elevated diaphragm and evidence of collapse in the right lower lobe (Fig. 3A).

Treatment consisted of re-instituting the breathing exercises with the CO_2 bag; mist. ammon. chlor., drachms 4 every 4 hours; posture with encouragement to cough and expectorate; and aerosol therapy consisting of 1 c.c. of epinephrine 1% and ephedrine 1% in proportion of 1:9, plus 40,000 units of penicillin in the aerosol solution every 3 hours 5 times a day. Within 24 hours the patient was clinically improved and had normal chest findings 4 days later. The chest film showed early improvement in 3 days, and complete clearing in 6 days (Figs. 3B and 3C).

Comment.—Inactivity postoperatively and difficulty in coughing due to the abdominal operation probably were the initiating factors causing the bronchial obstruction and atelectasis of the right lower lobe.

CASE 21

R.W., aged 14, male. Admitted to hospital with a diagnosis of bilateral saccular bronchiectasis. Under spinal anæsthesia the right middle and lower lobes were removed. He was given the routine spinal care and the CO_2 rebreathing bag postoperatively. He also received mist. ammon. chlor. drachms 4 every 4 hours five times a day; postural drainage; and aerosol therapy consisting

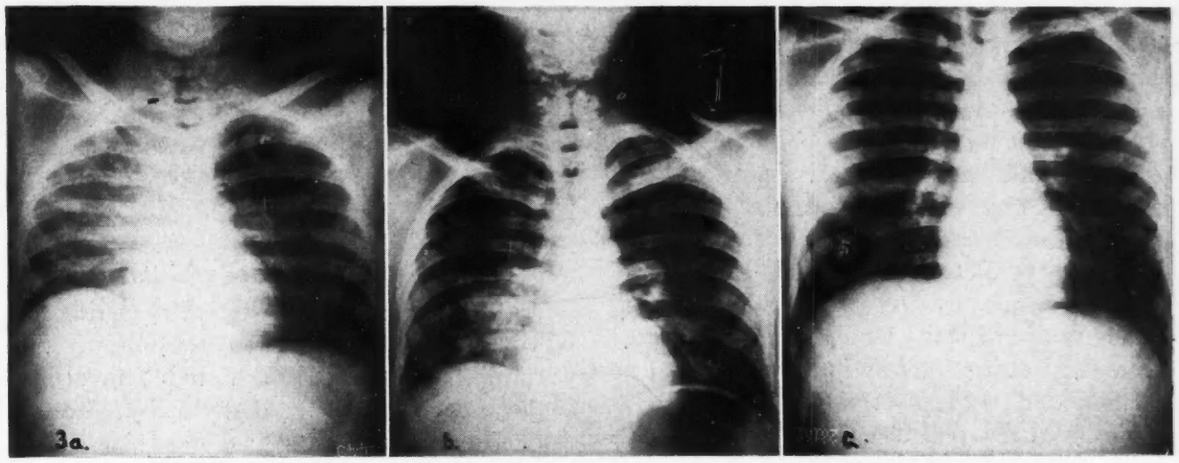

Fig. 3.—(A) Atelectasis in the right lung in a young male following appendectomy. (B) A chest x-ray of the same patient 48 hours after treatment was instituted. (C) The same patient six days later showing complete clearing of the shadows.

of 1 c.c. of neosynephrine 1% and 25,000 units of penicillin in the aerosol solution every 3 hours 5 times a day. He also received 50,000 units penicillin intramuscularly every 3 hours. For the first 5 days postoperatively he had a low grade fever of 100° and difficulty raising his sputum, partly due to chest pain. On the 5th postoperative day he became dyspnœic. Physical examination revealed absent breath sounds over the right upper lobe and the chest x-ray showed complete collapse of the right upper lobe (Fig. 4A). More vigorous treatment, particularly posture and encouragement to cough, was rewarded by the patient expectorating a large amount of retained sputum. Physical signs of aeration of the right upper lobe were almost immediate and a chest x-ray showing re-expansion was noted within 24 hours (Figures 4B and 4C). Thereafter his convalescence was uneventful.

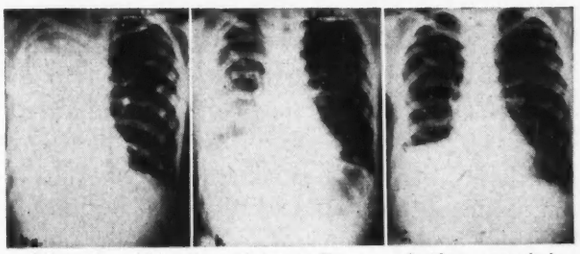

Fig. 4.—(A) Complete collapse of the remaining right lung following a lobectomy on the right side. (B and C) Progressive to complete re-expansion in the same case within 12 to 24 hours.

Comment.—Failure to evaluate the ominous difficulty of raising sputum and the low grade fever resulted in a sudden collapse of the right upper lobe. Quick logical treatment resulted in the release of the obstruction, with gratifying effects.

DISCUSSION

Routine prophylactic procedures are practised in most hospitals today to combat postoperative pulmonary atelectasis. This has resulted in a decreased incidence of this complication. When it does occur, the medical management should follow rational lines, as have been outlined above. All these measures contribute to release of the obstruction. Aerosol therapy with bronchodilator and vaso-constrictor drugs are added to the medical management of atelectasis. The authors feel this measure is of considerable value. Epinephrine 1% is frequently employed in the aerosol mixture to give a quick effect, which can be prolonged by incorporating ephedrine 1% in the same mixture. Barach[3, 4] and Segal[5, 6] through their clinical investigations showed that neosynephrine 1% has a markedly decreased toxicity in comparison with epinephrine or ephedrine. The drug can be used over long periods of time without adverse effects or the development of drug tolerance.

In practice it was found by repeated experience that the patient must be schooled very thoroughly and constantly in the proper production and application of the aerosol. This not infrequently goes on to the point of exasperation of the patient, or instructor, or both. It is important that the patient understands the technique if the therapy is to be beneficial. It is particularly impressed on the patient that the important time to be generating the aerosol is at the beginning of inspiration, thus ensuring that the mist reaches the deeper and more peripheral parts of the lung. This latter instruction is the basis of effective aerosol therapy in respiratory disease.

Relief of the bronchospasm with aerosol therapy facilitates the release of the mucous plug causing the obstruction in atelectasis. The patient appears to cough more easily and expectorate his retained secretions with less effort.

The series of cases presented is admittedly small but the authors feel that it is quite representative of the nature of the problem and a rational management of postoperative pulmonary atelectasis. There is a predominance of

cases which received pulmonary surgery and consequently these were more vulnerable to this complication. It is emphasized that all measures recommended, and not one alone, contribute to the successful management of atelectasis by medical means. Bronchoscopic aspiration is of great value and should not be denied to the patient when indicated. The less traumatizing measures by medical methods, as outlined above, are, however, usually successful, and more comfortable to the patient. The principles involved in bronchial obstruction and atelectasis must be understood and logically treated before successful results in the difficult cases can be expected.

SUMMARY

1. The problem and medical management of postoperative pulmonary atelectasis is discussed.

2. Twenty-three cases with this complication and management are outlined.

3. Excellent results were experienced by employing medical means for relieving atelectasis.

4. Bronchodilator drugs given by aerosol appeared to be a valuable adjunct in relieving the bronchial obstruction.

Our appreciation is expressed to Dr. G. Gavin Miller and the Surgical Staff of the Royal Victoria Hospital for the use of material on the surgical wards.

REFERENCES

1. ARONOVITCH, M.: *Canad. M. A. J.*, **53**: 222, 1945.
2. *Idem*: *Canad. M. A. J.*, **56**: 643, 1947.
3. BARACH, A. L.: The Principles and Practice of Inhalation Therapy, J. B. Lippincott Co., Philadelphia, 1944.
4. RICHARDS, D. W., BARACH, A. L. AND CROMWELL, H. A.: *Am. J. M. Sc.*, **199**: 225, 1940.
5. SEGAL, M. S.: *New England J. Med.*, **229**: 235, 1943.
6. SEGAL, M. S. AND RYDER, C. M.: *New England J. Med.*, **233**: 747, 1945.

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ELECTIVE SURGICAL INDUCTION OF LABOUR

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IT is frequently advantageous to both patient and doctor to carry out an elective induction of labour. Most physicians in Alberta doing maternity work have multiparous patients living some distance from hospital who during winter and spring have difficulty in getting to hospital in time over semi-impassable roads. Occasionally one encounters patients who are obviously overdue or at term and who are suffering acute discomfort from pressure symptoms. Others give a history of a previous precipitate labour, and injury to the fetus is feared if they are unfortunate enough to deliver without medical assistance. A fourth and smaller group are those patients near term with whom false labour pains assume all the unpleasant characteristics of real labour.

With such patients an elective induction may be considered, providing that the following important criteria are unquestionably present: a cephalic presentation; at term by size and calculation; a fully engaged head; no disproportion suspected; the cervix soft—in the case of primiparæ dilated 1 cm. and in the case of multiparæ, 2 cm.

Technique. — The above conditions being satisfied, the patient is admitted to hospital without breakfast on the morning of a prearranged date and given a saline enema. Following its expulsion, 10 c.c. of calcium gluconate is administered intravenously at the rate of 1 c.c. per minute. The patient is then prepared as for delivery and a simple rupture of the membranes is carried out under sterile technique with a partial ether anæsthetic. Amniotic fluid is allowed to run out slowly, being controlled by the operator's vaginal fingers until all that will flow out freely has been expelled.

If labour ensues within four hours as it almost invariably does there is no oxytocic used. If labour does not begin within this time limit a high hot enema is administered and pitocin one minim intramuscularly, given at 30 minute intervals until pains start or up to a maximum of six doses.

Two drugs honoured by time for use in induction of labour, castor oil and quinine, have been purposely omitted in this series and a relatively new one has been added, calcium gluconate. Castor oil was discarded as being of doubtful value and unpleasant to the patient. Quinine is not considered to possess any ability to cause effective contractions and in addition is felt to be capable of producing deafness in the newborn.

I cannot claim any originality in the use of this technique which has been described by R. M. Grier[1]. Prior to Grier's publication calcium gluconate had not been tried. His success with it prompted a trial and it is believed to be an

efficient stimulant to uterine contractility. Grier found it experimentally and clinically superior to œstrogens for this purpose.

Pitocin or pituitrin when used is given in one minim doses, as these have been found by experience to be equally effective and presumably less dangerous than the larger doses. It was necessary to use a stimulating oxytocic in less than 5% of cases.

RESULTS

This technique has been employed by the writer since October, 1947, on 162 cases. The cases were quite unselected except for the criteria above mentioned. Two were for therapeutic reasons in that they were primiparæ with heart disease (compensated). There was one case with severe toxæmia. One case was a failure due to poor judgment on the part of the operator, in that he allowed "family influence" to prompt him to attempt the induction on a poorly engaged head and rigid cervix. She went into labour after three days with no apparent ill effects.

Maternal morbidity was not startling. There were eight cases with fever over 100.4° F., one unexplained, three pyelitis, one mastitis, one upper respiratory infection and two with moderate parametritis. This represents an incidence of 6%. No case remained in hospital beyond the tenth day. There were in addition four afebrile patients who required treatment, two with phlebitis controlled by dicumarol and two with post-partum bleeding, one of whom required a curettage.

Fetal deaths numbered three; one died of erythroblastosis and one from cerebral hæmorrhage following a tentorial tear. The mother had an especially easy labour and delivery. She did not precipitate and the child's death came as a surprise. The third death was due to atelectasis. Fetal morbidity was represented by three cases—one of conjunctivitis, non-specific; one of congenital extrophy of the bladder and a third with unexplained fever.

It may be observed from Table I below that our results approximate those of Grier, the average latent period for primiparæ being 2¼ hours and for multiparæ 1¼ hours. The longest latent periods for primiparæ (with the exception of the failure mentioned above) were 8¼ and 6 hours (respectively). The longest latent period for multiparæ was 8¾ hours.

TABLE I.

	Average latent period	*Average duration of labour*
Primiparæ	2¼ hours	6½ hours
Multiparæ	1¼ hours	4¾ hours

The important observation from Table I is the corroboration of the impression that surgical induction materially shortens length of labour. This is true regardless of parity and is almost invariable. The longest labours for primiparæ in our series were 18¾ hours and 20 hours. They were both outlet dystocias. The longest labour for a multipara was 12 hours and this patient had pains of poor quality and an occiput posterior. It is interesting in this connection to note that standard textbooks give the average duration of labour for primiparæ as 18 hours and for multiparæ as 12 hours. Almost all the patients received sedation in the form of demerol and hyoscine. About 60% were delivered under low spinal anæsthesia the rest with partial ether. The two heart cases received heavy nupercaine 1:200.

DISCUSSION

The reaction of country patients to this innovation has been good. They are pleased not to have to wait about in hotels for the onset of labour and are freed of the worry of delivering on the way to hospital. City patients are enabled to engage help at home for a definite period instead of having to make hasty last-minute preparations. Most appreciate the fact that their labour is shorter.

In general, elective induction by this procedure is considered safe and in properly selected cases is justified to shorten labour and to provide a convenience for certain patients in special circumstances.

BIBLIOGRAPHY

1. GRIER, R. M.: *Am. J. Obst. & Gyn.*, 54: 511, 1947.
2. DIECKMANN, W. J. AND MCCREADY, R. B.: *Am. J. Obst. & Gyn.*, 54: 496, 1947.
3. SCHUMAN: Textbook of Obstetrics.
4. ROBLEE, M. A.: *Am. J. Obst. & Gyn.*, 53: 382, 1947.

RÉSUMÉ

L'auteur expose les avantages de l'accouchement provoqué dans les milieux urbains et ruraux. Une fois les conditions requises, remplies; la patiente reçoit un lavement suivi d'une injection de 10 cc de gluconate de calcium et de la rupture artificielle des membranes. L'auteur n'emploie ni la quinine ni l'huile de ricin. Les statistiques sont excellentes en autant que les cas sont bien choisis et les patientes sont reconnaissantes des facilités que cette méthode leur procure.

YVES PRÉVOST

THYROTOXIC HEART DISEASE*

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THIS paper is intended to discuss some of the considerations and clinical observations made by us on some of the various aspects of thyrotoxic heart disease and involves a partial analysis and review of 33 such cases. These cases were picked out of approximately 400 cases of toxic goitre that were observed during the period from 1943 to 1946 inclusive. Because thiouracil and some of its derivatives had not been much in use until 1946 we cannot, of course, make much comment about this drug in these cases, although four were treated with thiouracil. Of our 33 cases, 23 had persistent auricular fibrillation, 19 having thyroidectomy done, and 4 being treated with thiouracil; 8 cases had a normal rhythm preoperatively, but developed auricular fibrillation postoperatively; and 2 cases had manifestations of heart failure with a normal rhythm preoperatively, one being in congestive heart failure and the other in left ventricular failure associated with hypertension.

As well as this, several patients with heart murmurs were followed postoperatively for further study and observation.

TABLE I.

	Age incidence				
	30-40	41-50	51-60	61-70	71-80
Persistent auricular fibrillation	1	2	10	9	1
Postoperative auricular fibrillation—normal rhythm preoperatively ...	1	3	2	2	
Heart failure with normal rhythm				1	1
Total	2	5	12	12	2

From the above table, it will be noted that thyrotoxic heart conditions were seen chiefly in elderly people, the great majority being past the age of 50. In our group, 26 out of 33 patients, or 79%, were over 50 years of age, the oldest being 78 and the youngest 34. It is also of interest to note that with the routine preoperative preparation and the postoperative care that was used, all of these patients stood the operation well and made uninterrupted recoveries. There were no operative deaths in our series, 11 being over 60 years of age and two over 70.

As to sex preponderance, there were 21 females as opposed to 12 males, an incidence of almost 2 females to 1 male.

It has been our experience that the majority of thyrotoxic heart disease is found with adenomatous goitre and often with adenoma or adenomata showing degeneration. Thus, in our series 25 cases, or 76%, had adenomatous goitres and of these, in the 21 cases operated on, well over half showed evidence of degeneration in the adenomata to be present. In our series, then, adenomatous goitre is *the* type of goitre associated with thyrocardiac disease and this has suggested to us that there may be some other reason rather than chronic hyperthyroidism which causes the heart condition found with the goitre in these cases. This further suggests that in our opinion there may be a dysfunction rather than a hyperfunction of the gland in these cases and as we will point out later on (in discussing case histories) several of these patients, though their basal metabolism was within normal or borderline limits, did not stop fibrillating until their goitre was removed. However, we might note at this point that there is still considerable disagreement among many of the authorities as to whether there is an actual hypersecretion as opposed to an abnormal secretion of the thyroid gland in these thyrocardiacs. Thus, Hertzler believes in the distinct entity of "cardiotoxic goitre" which he defines as "one that causes a disturbance of the heart by a toxic substance released by degenerative changes in the thyroid". Lahey, on the other hand, believes that all true thyrocardiacs have actual hyperthyroidism *per se*. Our opinion based entirely on clinical experience with these cases favours the former view, namely, that there is an actual toxic substance released by the thyroid.

As regards the basal metabolism, it is interesting to note that in quite a few of these cases, as stated above, it was not grossly elevated. Thus, as is evident from the table below, 11 patients with adenomatous goitre, or 45%, had basal metabolic rates below 35%.

* Presented at Staff Meeting, Winnipeg Clinic, October 13, 1948.

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TABLE II.

Basal metabolic rate (in % above 0)	*Adenomatous goitre*	*Diffuse toxic goitre*
Below 15	1	
15-25	6	
26-35	4	
36-45	1	2
46-55	5	2
56-65	2	3
Over 65	4	2

One must also remember that in these cases there may be coexisting organic heart disease present, particularly arteriosclerosis and hypertension in the older age group, which in itself may be "latent" or producing no signs or symptoms. However, here, the added burden of the thyrotoxicosis may produce cardiac signs or symptoms such as cardiac irregularities or angina pectoris which may be relieved by removal of the thyroid. This will be seen in several of our cases which are quoted at the end of this paper. Means believes that in every thyrocardiac *with failure* "the failure is produced by the advent of thyrotoxicosis in a person with an already damaged heart"—either rheumatic heart disease in young people or hypertension and arteriosclerosis in the older age group. Removal of the thyrotoxic state may relieve the failure in these cases.

Cardiac irregularities.—As has already been seen, the most common cardiac disturbance in these patients was auricular fibrillation. Thus, 23 cases had persistent auricular fibrillation prior to therapy, 4 of these being in congestive heart failure as well. Nineteen of these cases had a thyroidectomy and of these, 10 cases, or over 50%, stopped fibrillating spontaneously following their operation. Probably the incidence was even higher than this, as in 3 patients we were unable to get follow-up examinations after 3 weeks. It is not possible to state exactly how long it took for the fibrillation to stop in every case, as some of these patients left a week or two after their operations and were not seen again for 2 or 3 months' time. However, the time interval varied from one day to several months postoperatively.

The 4 patients who were not operated on were kept on thiouracil or propyl-thiouracil. Only 1 of these 4 regained and maintained a normal rhythm. In the other 3, the fibrillation persisted in spite of maintaining their basal metabolic rates around normal levels for 6, 10 and 18 months respectively. It might be noted at this point that in 3 of our operative cases, the basal metabolic rate was brought down to normal levels with the use of thiourea and thiouracil, but fibrillation did not stop until after thyroidectomy was done. One of these cases will be quoted here:

Mr. H.A., aged 52. Examination revealed auricular fibrillation, rate 170 with a soft systolic murmur at the apex. The heart was enlarged slightly on the x-ray. Electrocardiogram revealed rapid auricular fibrillation with an inverted T wave in lead CF4. There was a diffuse goitre present and the basal metabolic rate was plus 73%. There was marked loss of weight, tremor, etc., present and this patient was considered to be very toxic.

Treatment.—December 1 to 11. He was given Lugol's solution min. xv three times daily, but did not improve sufficiently to perform thyroidectomy.

December 11. Placed on thiouracil and the basal metabolic rate was brought down to plus 17% in about four weeks' time and kept there.

February 14. About two months after being on thiouracil, the right lobe and isthmus were removed. The patient was still fibrillating and was kept on thiouracil.

February 23. The basal metabolic rate was minus 2% and it was kept at this level.

March 6. Approximately three months after first being placed on thiouracil the left lobe was removed. Thiouracil was discontinued at this time.

March 16. The patient was still fibrillating on discharge. He went home and was not seen again until seven weeks later (May 2) when his heart was found to be regular, the systolic murmur was gone and the heart was normal in size. The basal metabolic rate was minus 9% at this time.

Thus, it would appear that in some cases at least, in which fibrillation does not stop while on thiouracil, subtotal thyroidectomy might produce the desired effect.

Eight cases in our series had regular hearts before operation, but developed auricular fibrillation postoperatively. In every case this reverted back to normal rhythm in one to three days' time.

Heart size and murmurs.—It will be noted that 60% of our series had some enlargement of the heart and of the 23 cases with persistent auricular fibrillation 16, or 70%, had some cardiac enlargement. This was determined in every case by x-ray examination and in many cases the enlargement was very slight and did not conform to any definite pattern. In some of these, where the auricular fibrillation stopped postoperatively, the heart returned to normal size (as in the case quoted above). However, our main guide as to the presence of organic heart disease in cases with cardiac murmurs was often the size and shape of the heart for, unless the heart was definitely enlarged clinically as well as by x-ray examination, and particularly if the

TABLE III.

Type of case	*No.*	*Heart enlarged*	*Heart not enlarged*
Persistent auricular fibrillation	23	16	7
Postoperative auricular fibrillation—normal rhythm preoperatively ..	8	3	5
Normal rhythm—heart failure	2	1	1
Total	33	20	13

enlargement did not conform to the pattern of valvular disease, we were reluctant to assume that the murmur was an organic one. The reason for this was that in many of these cases murmurs may be heard which in some instances may be thought to be due to organic heart disease only to find that they disappear postoperatively. Indeed, Means has stated that "the heart in thyrotoxicosis may give physical signs typical of organic disease and yet later anatomic investigation may reveal an entirely normal organ" and he quotes a case of hyperthyroidism in which a diagnosis of mitral stenosis was made because of the presence of an apical diastolic murmur; yet some years later anatomic examination of the heart revealed it to be normal.

In many cases where murmurs were present preoperatively and persisted after operation, we assumed that they might be organic, but again unless the heart was enlarged at the same time we were hesitant in assuming that they definitely had an organic basis.

Preoperative treatment.—Iodine in the form of Lugol's solution 10 to 15 minims three times daily for 12 to 14 days preoperatively was used in all the patients in our series. As stated previously most of our patients did not have the benefit of the anti-thyroid drugs and these were used in the form of thiourea or thiouracil preoperatively in only three of our cases. In these three cases the metabolism was brought down to normal limits and then about two weeks before operation, Lugol's solution was administered concomitantly.

The damaging effects of thyrotoxicosis on the liver have been stressed by many, and a few authorities even favour the idea that acute hepatic failure is the underlying basis of thyroid crisis. Since the ability of glucose to protect against liver damage is well established and a liver high in glycogen content withstands damaging procedures far better than one depleted of glycogen, one of our main considerations in the preoperative treatment was therefore to load up the liver with glycogen. Hence, our patients were all given a high carbohydrate, high protein, high caloric diet and glucose drinks were forced at all times, particularly preoperatively. In addition, immediately pre- and post-operatively, these patients were given glucose intravenously at a very slow rate to insure adequate mobilization of the glucose by the liver and also heart muscle. Vitamin B complex was also given in large doses, 19 mgm. of thiamine chloride being given daily, as an aid in restoration of damaged liver function.

Regarding the hippuric acid test, which has been recommended by some as a test of liver function to use as an indication as to whether the patient is ready for operation or not, we might say that we have not found it satisfactory. The chief reason for this was that the results were so widely variable and fluctuant and were entirely dependent on the immediate status of the glycogen content of the liver; the result could be changed in 24 hours by loading up the patient with glucose and vitamin B. After a trial period, we abandoned its use and every patient was treated preoperatively as if liver damage was present, as described above.

Quinidine was not used preoperatively and the use of digitalis was avoided except if congestive heart failure was present.

Postoperative treatment.—All our patients were given sodium iodide intravenously as well as glucose postoperatively. Lugol's solution was administered in decreasing dosage for variable periods of time.

Regarding the use of digitalis we felt that it was neither useful nor safe in thyrotoxicosis, and that it had little or no effect on cardiac function. This was particularly so in the postoperative cases where the temperature was elevated and the effect of the digitalis thereby largely nullified. The "toxæmia" in these cases, if it can be called that, seemed to counteract the therapeutic effect of the drug and, if to this was added a high temperature, the usefulness of the drug seemed to be extremely debatable. We found that all cases with a fast pulse and/or cardiac irregularity postoperatively, if left alone and given sodium iodide intravenously, did just as well and even better than those given large doses of digitalis or any of its derivatives. In these cases we always watched for evidence of congestive heart failure, particularly the pres-

ence of râles in the lung bases, as this was used as the indication that supportive heart therapy was required. However, in our cases this occasion never arose postoperatively and all of these patients recovered and did well without the use of digitalis. So that, in all our patients that developed very rapid auricular fibrillation or a rapid pulse immediately postoperatively, digitalis or its glycosides were not used in the absence of congestive heart failure. It is also interesting to note that all patients attended by us who developed auricular fibrillation for the first time postoperatively reverted to normal rhythm spontaneously in 1 to 3 days' time with the use of no medication except iodine and intravenous glucose.

As stated previously, over 50% of patients with auricular fibrillation before operation stopped fibrillating spontaneously postoperatively. Owing to this, and because of the risk attached, quinidine was not used in any of our cases postoperatively. It is interesting to note that in a report recently (1943) by Lahey, Hurxthal and Driscoll they have noted that, even though they have not employed quinidine sulphate as much during their last five years as formerly, yet the percentage of persistent auricular fibrillation postoperatively remained fairly constant. They state that "this would suggest that, while quinidine postoperatively promptly restores normal rhythm, in most instances normal rhythm would have recurred spontaneously later. On the basis of this experience the value of quinidine sulphate for thyrocardiacs can be questioned, and since the drug is toxic and must be given with caution, we doubt whether its use is as advisable as we formerly believed". Several cases from our series are quoted below:

CASE 1

Mrs. P.R., aged 70. This was a doctor's wife with a large degenerating adenomatous goitre, who had been "sick" and run-down for a number of years, with symptoms of heart failure of about one year's duration, namely, dyspnœa, ankle œdema, etc.

Examination revealed a very thin, sick looking, elderly woman whose weight was 85 pounds. The heart was fibrillating at 120 beats per minute. There were no murmurs. There was some enlargement of the heart evident on the x-ray with atherosclerosis of the aortic arch. The electrocardiogram showed only auricular fibrillation with no other significant changes. Congestive heart failure was manifested by the presence of ankle œdema, venous congestion, etc. The basal metabolic rate was only plus 27% and this in the presence of some heart failure. The congestive heart failure was treated with digitalis, mercurials, etc. However, the digitalis failed to slow the pulse appreciably. Accordingly, the digitalis was discontinued and the patient was given Lugol's solution 15 min. three times daily for two weeks preoperatively.

Fifteen days after her operation, her fibrillation stopped while on no medication besides Lugol's and her pulse has been regular ever since (three years). Her failure cleared up entirely and her cardiac reserve improved tremendously. As well as this, she gained up in weight from 85 to 121 pounds in one year and was able to carry on with normal activities again, and the change from a thin, sickly, elderly woman in heart failure into a robust, cheerful and comparatively healthy individual was indeed most dramatic to watch.

In this case, in spite of the age, as far as we could determine, degenerative arteriosclerosis, although present to some degree, was not playing much of a part in the cardiac condition and the proof of the matter was the change to a normal rhythm and the restoration of a normal cardiac function for the age following thyroidectomy. Also this case illustrates the insidiousness of this type of goitre, the fact that cardiac disturbances often dominate the picture, and that this type of nodular goitre may affect the patient markedly, but affect the basal metabolic rate very little.

CASE 2

Mrs. J.B., aged 50. This patient had a definite history of angina of effort and this was actually the only presenting complaint.

Examination revealed the presence of a large adenomatous goitre. Basal metabolic rate was plus 83%. The heart was regular, with a rate of 100. There was a fairly rough systolic murmur heard at the base and a soft blowing diastolic murmur just to the left of the lower border of the sternum inside the apex. The heart was normal in size on the x-ray and an electrocardiogram revealed the presence of left ventricular strain. Blood pressure was 220/115. The Master 2-step test for coronary insufficiency was positive.

March 27. Thyroidectomy (subtotal) done.

March 29. Auricular fibrillation developed at a rapid rate.

March 30. Pulse regular and remained so (no medication except for iodine).

Three weeks postoperatively, the systolic murmur at the base of the heart was unchanged, but the diastolic murmur was *not heard*. The blood pressure was 220/110. The angina of effort had disappeared and the Master 2-step test was now negative.

This case, then, demonstrates that a thyrotoxic state may bring to the surface a "latent" coronary artery disease, in this case manifested by the presence of angina pectoris, and that following thyroidectomy this condition may again assume "latency". Also, it is interesting and important in this case to note the disappearance here of the diastolic murmur following operation, without any change of the blood pressure.

CASE 3

Mr. M.J., aged 68. First examination, July, 1945. At this time patient complained only of an attack of numbness in his left arm. Examination revealed the presence of a large adenomatous goitre. The heart was regular, with a rate of 56. Blood pressure was 240/104. The heart was enlarged to the left on the x-ray and the electrocardiogram showed the presence of chronic left ventricular strain and myocardial damage. Basal metabolic rate was plus 12% and ten days later it was rechecked and found to be minus 16%. The goitre was considered to be non-toxic.

Second examination, March, 1946. Symptoms of heart failure present, namely, dyspnœa, orthopnœa, etc. The heart was fibrillating at a rate of 180. The basal metabolic rate was plus 38%. The patient was hospitalized and digitalis in full doses failed to produce sufficient slowing of the heart. Lugol's was then given ten days preoperatively.

April 8, 1946. Thyroidectomy (subtotal).

April 24, 1946. Discharged, still fibrillating. The patient went home and did not return until May 20, 1946, at which time the fibrillation had stopped. The blood pressure was 213/115.

Last examination, August, 1947. Pulse regular at 70. The heart was enlarged on x-ray. Blood pressure was 250/110. The electrocardiogram revealed no change from that of July, 1945.

This illustrates a case of rather severe hypertension with changes in the electrocardiogram interpreted as indicating the presence of myocardial damage. It was very difficult here to determine with certainty preoperatively just how much of a rôle the goitre was playing in the production of the signs and symptoms, as here again the cardiac manifestations were the predominating ones and in this instance could have been ascribed to the presence of hypertension, coronary heart disease and myocardial damage. However, the presence of a thyrotoxicosis was again proved by the reversal to a normal rhythm and marked improvement in cardiac function with disappearance of any heart failure following thyroidectomy, even though the blood pressure and electrocardiogram were both unchanged by the latter procedure. This in turn demonstrates how an insidious onset of a thyrotoxic state may overburden a heart which is already damaged to produce cardiac irregularity and variable degrees of heart failure, both of which may be improved, without affecting the cardiac damage already present by removal of the thyrotoxicosis.

CASE 4

Mrs. J.M., aged 62. Examination revealed a large adenomatous goitre. Basal metabolic rate was plus 32%. There was a history of some weight loss. Examination of the heart revealed it to be fibrillating at between 70 to 80 beats per minute. There were no murmurs present. The heart was enlarged to the left on the x-ray and the electrocardiogram revealed left axis deviation, auricular fibrillation, and possible slight digitalis effect (patient had been getting digitalis from her family doctor previous to admission).

This patient was kept under observation for two to three weeks to allow any digitalis effect to disappear, but the apex rate remained at the same level, *i.e.*, between 70 and 80. After being on Lugol's for 12 days, a thyroidectomy was done on January 22. On discharge in February, the patient was still fibrillating slowly. In May, a report was received from the family doctor that the pulse was regular and that the patient had gained in weight and felt immeasurably improved.

Although the pulse rate is usually rapid, this case was characterized by an unusually slow pulse rate with auricular fibrillation that was caused by a thyrotoxicosis. Here again, the cardiac manifestations were the predominating ones and the basal metabolic rate not grossly elevated.

CASE 5

Mrs. K.O., aged 43. Basal metabolic rate plus 81%. Diffuse toxic goitre (Graves' disease). Examination of the heart showed it to be regular, rate 140, normal size, systolic murmur at the apex with the suggestion of a thrill.

Examination 6 months postoperatively. Heart normal in size, murmur and thrill gone.

This case illustrates how careful one must be in evaluating any murmur or thrill in the presence of a thyrotoxicosis as in the above case both disappeared following thyroidectomy.

SUMMARY

A few observations on thyrotoxic heart disease based largely on clinical experience have been noted. A partial review and analysis of 33 cases of thyrotoxic heart disease seen from 1943 to 1946 inclusive and some of the more interesting cases have been presented.

BIBLIOGRAPHY

1. HERTZLER, A. E.: Diseases of the Thyroid Gland, Paul B. Hoeber, Inc., N.Y., 1941.
2. GREENE, A. M. AND HURXTHAL, L. M.: *New England J. Med.*, **225**: 811, 1941.
3. MEANS, J. H.: Thyroid and Its Diseases, J. B. Lippincott Co., Pa., 1937.
4. SCHMIDT, C. R. AND HERTZLER, A. E.: *Endocrinology*, **31**: 684, 1942.
5. LAHEY, F. H., HURXTHAL, L. M. AND DRISCOLL, R. E.: *Ann. Surg.*, **118**: 681, 1943.

Erratum

In our account of the British Commonwealth Medical Conference at Saskatchewan which appeared in the August issue, Dr. J. A. MacFarlane, Dean of the Faculty of Medicine in the University of Toronto, was referred to as Professor of Surgery. This was in error. The Professorship of Surgery in that university is held by Dr. R. M. Janes.

RECONSTRUCTION OF DIGITS OF DEFORMED HANDS

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DURING the past war a legacy of mutilated hands was bequeathed to those interested in their repair. These were the result not only of war wounds but in many instances were caused by industrial accidents, particularly in those factories assembling flares and small arms ammunition. Since the hand is the most important unit of the upper extremity most of these patients' requests for plastic surgery were due to a desire for functional improvement, a better esthetic appearance, or a combination of both factors.

The most frequent need was for restoration of pinch function to the crippled hand by reconstruction of an opposition digit. In a normal hand the "pinch" function requires three essentials: (1) The thenar muscles must be present and active in a state of functional integrity, attachment and innervation. (2) There must be an adequate length of projecting thumb. (3) There must be suitable length of finger or fingers to which the thumb can be brought into contact in the movements of opposition and flexion. Many of the injured hands may reveal loss of one or more of the above factors but provided the first condition is satisfied their pinch function can be restored. As in many other phases of plastic surgery an attempt to repair the defect in the shortest possible time does not always achieve that objective, due to complications and extra stages which arise solely as the result of ill advised haste. Therefore the timing and sequence of steps should be checked carefully to reduce the element of risk to a minimum. We have been interested in the repair of these injuries for some time and a variety of commonly encountered types of mutilated hands has been selected to illustrate the use of a simple method of restoring to a very considerable measure the function of a traumatized hand without increasing the deficit of fingers and with little risk of the development of complications in the course of the reconstruction.

RECONSTRUCTION OF THUMB

Loss of the thumb reduces the efficiency of a hand by about 50% and is approximately equivalent in terms of function to loss of all fingers of a hand. Opposition is a complex movement and takes place at the radionavicular, intercarpal, carpometacarpal and metacarpophalangeal joints. It can be divided into two main movements; one which takes place mainly in the carpometacarpal joint, and the second which is a flexor movement at the metacarpophalangeal joint. Many different types of operation for restoration of opposition or pinch of a hand have been devised.

1. Phalangization or deepening the web between the thumb stump and metacarpal of the index finger is a simple procedure. The cleft which is thus created can be used by the patient and its value can be assessed in terms of function. An advantage of this method is that all the nerve endings of special sensation are retained and sensory perception is more acute. The functional value of the procedure is proportional to the length of the remnant of the thumb.

2. Nicoladoni's operation in which a toe with its tendons, phalanges and joints intact is transplanted to the thumb stump by a pedicle flap technique, is not employed so much now as it has been in the past. It involves a prolonged and trying pretzel-like posture during a series of transfer operations. Review of a number of these cases many years after successful transplantation revealed that a large percentage were anæsthetic, stiff or could not be tolerated by the patient.

3. Transplantation of a contralateral digit has been employed in some cases. Technically it is more difficult, the finger may be lost during transfer or it may gradually become stiff and non-functional over a period of years. Should either of these mishaps occur, not only must a new reconstruction be planned, but it must be emphasized that the donor hand has suffered partial mutilation.

4. An increase in the length of a thumb stump can be achieved by the advancement of local skin flaps and insertion of a bone peg for support if no excessive scarring is present. While the nerve supply may be interrupted temporarily there is every probability that sensation will return with a high degree of normalcy due to the fact that the local flaps

possess highly specialized nerve endings into which the nerve fibres can grow. Unfortunately the condition of the skin about the stump may be so damaged by the original trauma or the stump may be so short that insufficient skin is present to employ this method.

5. Pollicization involves the transfer of an index finger to the thumb stump. If successfully carried out this method restores opposition, a strong grip and normal apposition. It should be differentiated from the more difficult surgical problem in which the thumb has been totally destroyed. In this variety of injury, pollicization will restore the lost prehensile action without power of opposition. Many surgeons believe that pollicization of an index finger should be limited to those patients who have suffered an associated partial loss of the index finger. Cuthbert has shortened a pollicized index finger by resection of bone from shafts of the first and second phalanges. However, the soft tissues were not readily adapted to the shortened bony framework. Moreover, there are several other disadvantages inherent in this procedure. First, by this operation the palm is narrowed and some strength of grip is inevitably lost. Second, the hand which is already esthetically unattractive is depreciated further. Indeed, it has been noted that some patients have requested that the deep cleft created between the index and middle finger be camouflaged by the insertion of a pedicle flap. Finally in spite of all precautions, some complication may arise which will either decrease function or result in loss of the digit. Thus much may be lost without gain.

6. Lengthening of the thumb by means of a tubed pedicle flap and bone graft has many advocates and this method has been widely employed during the last war by plastic surgeons. This method is most useful: (*a*) If sufficient metacarpal stump is left with the thenar muscles in a functioning state of attachment, integrity and innervation. (*b*) When the index finger is intact. (*c*) If there is present or can be constructed an adequate length of finger or fingers to which the rebuilt thumb may be apposed in the movements of opposition and flexion. Many variations in the stages of reconstruction have been tried but the following sequence is considered to be associated with the minimum risk. (1) Preparing a tube pedicle. (2) Attachment of pedicle to hand. (3) Severing of pedicle from abdomen. (4) Insertion of bone graft. A tube pedicle of adequate length and circumference equal to the normal thumb is prepared in a convenient position on the abdomen or pectoral region which is relatively free from hair. The tubed portion need only be slightly longer than the length of extension required unless the reconstruction of other digits is contemplated. Little fat should be included in the pedicle so that the bone graft which is to be inserted later may be more easily accommodated and because we believe that nerve regeneration in the pedicle occurs more completely when little fat is present. The adequacy of the blood supply may be estimated by occluding one end of the pedicle with a rubber band and when it is satisfactory the appropriate end is severed. All scar tissue about the stump is excised and an extension is carried down one side to avoid a ring scar and consequent poor circulation. Failure to obtain a good length of attachment to the stump may account for many of the reports of poor healing of the free end of the repaired thumb. It is desirable to conceal the linear suture scar of the pedicle by having it face medially in the interdigital cleft and easy access is obtained through the scar for insertion of the bone graft. Any sloughing at this stage by forming a constricting scar jeopardizes the future result.

Severing the pedicle from the abdomen should not be attempted without clamping the base of the pedicle for increasing periods with a rubber band to develop a rich blood supply from the thumb stump. When the pedicle can be constricted for some time without becoming cyanotic, it may be severed without fear of development of a terminal slough or failure of primary healing which are frequently reported but avoidable complications. The free end is trimmed to form a rounded extremity and the wound is closed with stainless steel sutures. Until the bone graft is inserted a light moulded acrylic or similar type of splint is worn to support and protect the pedicle from trauma. When sound healing of the free end has occurred the next stage, that of inserting the bone graft, may be planned. The longitudinal suture line of the pedicle is reopened from one-half inch proximal to the end, down to the junction of the pedicle flap with the stump. The bone

stump is exposed, sclerotic material trimmed away and a hole drilled in its medulla to receive the pointed graft. The latter may be obtained from the iliac crest, fibula, tibia or rib according to choice. One end is fashioned as a peg which is morticed into the stump of the metacarpal or phalanx. The sides and opposite end are rounded. Chips of bone may be arranged about the proximal end of the graft to strengthen the line of union or augment contour. The thumb is then splinted in correct position. After four or five weeks active exercises may be started but a protective splint should be worn in the intervals until bony union is solid. A U-shaped inset may be made on the dorsum of the thumb

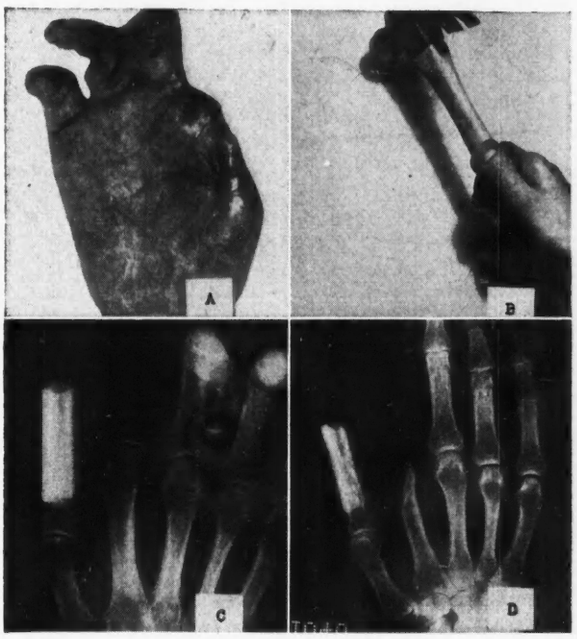

Fig. 1.—(A) Extensive damage caused by an electrical burn. (B) Four years after reconstruction during which the patient has continued his former work as an electrician. (C) Appearance of fibular graft two months after insertion. (D) Firm union and no evidence of loss of length of the graft after four years of active service.

to support an artificial nail which is cemented in place when desired.

CASE 1

W.P., a 35-year old electrician was admitted because of a severe electrical burn involving the right hand and thigh. After separation of necrotic tissue the thumb was lost as far as the metacarpophalangeal joint with the exception of a thin peg of bone which represented the remains of the proximal third of the first phalanx. The index finger was completely destroyed and there was a flexion contracture of the middle finger (Fig. 1A). A pedicle flap was prepared on the right side of the abdomen. The lateral end was delayed and then was attached to the stump at the same time as a shaped bone graft from the right fibula was pegged over the phalangeal stump. Due to the excellent blood supply both bone and pedicle flap healed rapidly. During this period the medial end of the pedicle was clamped at regular intervals for increasing periods of time. Consequently when the free end was severed and trimmed a few weeks later, healing per primam occurred. The supporting splint was removed when bony union was solid and a thick split graft was used to relieve the contracture of the middle finger (Fig. 1C). Four years later, the sensations of touch, pain, heat and cold were restored over the entire reconstructed thumb. Two-point discrimination did not return. The changing appearance of the bone graft over a period of four years in response to functional demands is shown in Fig. 1D. The patient has returned to his regular work and is satisfied with the amount of manual function which has been restored (Fig. 1B).

CASE 2

S.P., a 14-year old boy was admitted because of the congenital absence of both thumbs (Figs. 2A and 2B). Small tags of skin which represented the only evidence of an attempt to form normal thumbs, had been removed a few weeks after birth. His parents emphatically insisted that the normal digits should not be disturbed in any way by attempts at reconstruction of his thumbs. Accordingly a tube pedicle flap was raised on the abdomen and each was subsequently attached to the normal site of the thumb. The pedicle was then divided, leaving one half attached to each hand and the free ends were closed. At the next stage a peg-shaped graft from the right fibula was driven into the first metacarpal bone of each hand and the pedicle flap closed. The correct position of the pedicle was maintained for six weeks by a plaster cast. The postoperative appearance of the thumbs may be seen in Figs. 2C and 2D. It should be noted that the thumbs do not interfere with complete flexion of the fingers. A powerful grasp and pinch function has been obtained without depriving the hands of the normal function of the index fingers and without detracting from the cosmetic appearance of the hands. Increased function has been added without loss. The thumbs cannot be opposed but the increased agility of the digits easily compensates for this lack. Sensation is developing rapidly and will most probably reach the stage obtained in Case 1.

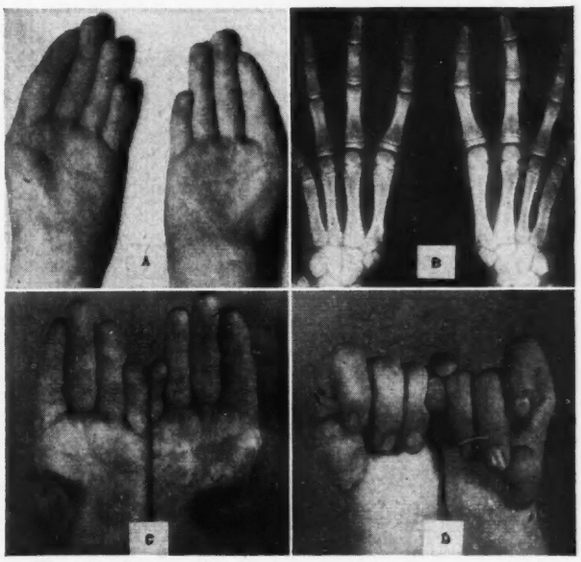

Fig. 2.—(A and B) Congenital absence of both thumbs. (C and D) Restoration of grasp and pinch function without narrowing the width of the palm.

RECONSTRUCTION OF DIGIT

In this instance the same stages were employed as in the construction of a thumb. A good length of attachment to the stump and a diameter of pedicle equal to that of the same

finger of the opposite hand were obtained. The length should be varied, depending on whether a predominantly cosmetic or functional effect is desired. If more than two phalanges are being restored it is important to fashion a curved bone graft which will simulate the finger in the position of grasp, thus the patient will not complain of it being in the way and its functional value will be increased. In view of the difficulty of transplanting nails, we have resorted to the use of artificial celluloid or acrylic nails glued with adhesive cement into previously prepared U-shaped depression. A typical case of reconstruction of a middle finger is shown in Figs. 3A and 3B. The patient had developed a marked inferiority complex as a result of the deformity. With the exception of a small area

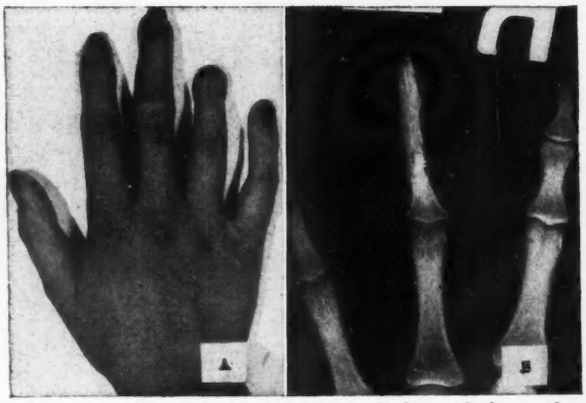

Fig. 3.—(A) Restoration of missing phalanx for cosmetic and psychologic reasons. (B) Rib graft dowelled and wired in position.

one-half centimeter in diameter at the tip of the finger, there was complete return of all sensation except two-point discrimination.

RECONSTRUCTION OF MUTILATED HAND

The reasons which bring a patient with a crippled hand to the surgeon are, first, a desire for a more useful hand, second, a better looking hand, and third, elimination of painful areas. While a patient will be grateful for improvement of function, women especially will complain if it is achieved at the expense of appearance. Fortunately the two usually accompany each other. Hands from which most or all of the digits have been lost can be rendered quite useful and esthetically more attractive by multiple tube pedicle restorations, provided a mobile remnant of the first metacarpal bone is present. One mobile digit on the thumb stump and at least one fixed or mobile extension from the palm can be made on the principles already described and represent the minimum functional improvement desired. Should a fragment of the first phalanges of the digits remain, the bone grafts may be pegged into these and a wider range of mobility of the fingers may be obtained. Depending on the requirements of each case either a long tube pedicle may be raised and transferred from stump to stump leaving appropriate lengths attached to each, or several pedicles may be raised in series on the abdomen and attached to the stumps simultaneously. The following case illustrates the need for both functional and esthetic improvement in a badly mutilated hand.

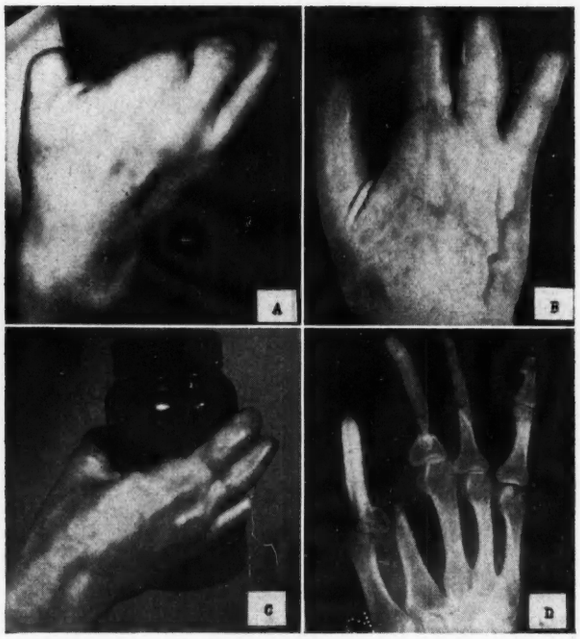

Fig. 4.—(A) Useless stumps of fingers of right hand following accident. (B and C) Good function of hand with grasp and pinch restored. (D) Appearance of fibular graft to thumb and rib grafts to third and fourth fingers one year postoperatively.

CASE 3

M.P., a 28-year old woman attached to the R.C.A.F. who suffered the loss of most of the right thumb, index, middle and ring fingers and the tip of the little finger. The hand was quite useless and the patient had developed a marked inferiority complex as a result of the deformity and insisted on cosmetic as much as on functional improvement (Fig. 4A). The only procedure which the patient would consider and which indeed was thought to be suitable was reconstruction with tube pedicles and bone grafts. A long tubed pedicle flap was raised on the abdomen. One end was attached to the thumb stump and the opposite end was attached successively to the stumps of the proximal phalanges of the middle and ring fingers. The head of the second metacarpal had been severed when the accident occurred and reconstruction of the index finger was not considered to be worthwhile. A bone peg for the thumb was obtained from the right fibula and curved grafts for the middle and ring fingers were obtained from the right tenth rib (Fig. 4D). Healing per primam without complication occurred in each instance. The patient is satisfied with the improved appearance of the hand and is able to perform

household duties (Figs. 4B and 4C). The return of sensations of touch, pain and temperature into the pedicles of all digits was complete. As observed in all other cases, two-point discrimination was absent. The objection frequently raised by some surgeons to the use of pedicles, because of repeated injury due to lack of sensation, has not been observed in any of our cases. We take special precautions to protect the digit from trauma while reinnervation is taking place.

CASE 4

K.L., a 26-year old soldier had both hands severely crippled when a Japanese grenade which he had picked up, exploded. Both thumbs were partially lost and the stumps were sensitive to light pressure. The dorsum of the left hand was extremely painful on light touch and the second and third metatarsals were covered with thin scar tissue over the distal portions (Figs. 5A and 5B). To provide a soft resilient covering, a pedicle flap was raised from the abdomen and used to cover the scarred area on the dorsum of the left hand and in the web space between the index finger and thumbs. The free end of the same pedicle was then used to provide a cover for each thumb stump (Figs. 5C and 5D). This patient is able to work as an unskilled labourer.

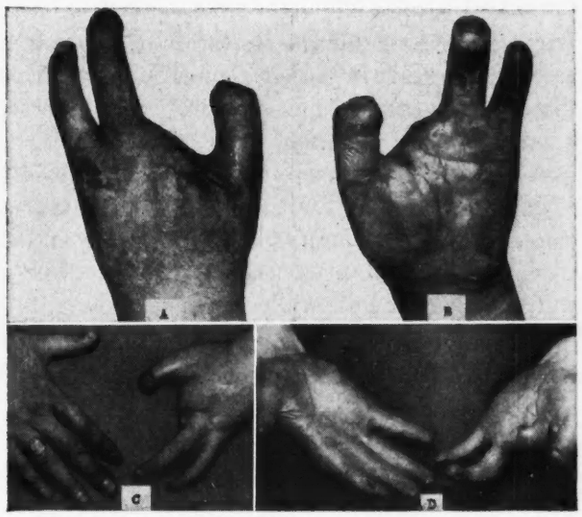

Fig. 5.—(A and B) Thin scar tissue covering bony stumps. (C and D) Padding to cover metacarpal stumps and thumbs provided by means of a pedicle flap.

CASE 5

T.L., a 20-year old woman employed in a munitions plant suffered very severe burns of the face and right upper extremity when a magnesium flare she was assembling exploded. The hand was charred and disarticulated at the radio-ulnar joint. The entire right arm required skin grafting (Fig. 6A). The thin atrophic stump of the forearm could not carry a prosthesis, so an open pedicle flap was wrapped about the stump after removing the skin graft; she was then ready to be fitted for a prosthesis (Fig. 6B).

SUMMARY

1. The x-ray appearance of bone grafts from the fibula and rib show their remarkable vitality, resistance to infection and ability to obtain an adequate blood supply. In each case the original length of the graft has been maintained for periods of time up to four years. In some cases structural changes have occurred as a result of functional demands.

2. The final extent of sensory return over periods of months has been remarkably complete in most of the cases. In one patient insufficient time has elapsed to permit complete reinnervation to the tip of the thumbs although it already had extended distally over half the length of the pedicle. In the other case a small area of anæsthesia about the size of a bean remained at the tip of the digit. The degree of regeneration depends to a considerable extent on complete removal of scar tissue and attachment of the pedicle well below the tip of the stump.

3. Several patients showed hyperæsthesia to pinprick in certain areas of the pedicle. It is important that the pedicle should be carefully protected until sensation has returned so that unnecessary scarring is avoided.

4. The functional improvement is dependent not only upon the surgical procedure chosen but to a considerable degree upon the determination and need of the patient to make the best use of the restored part.

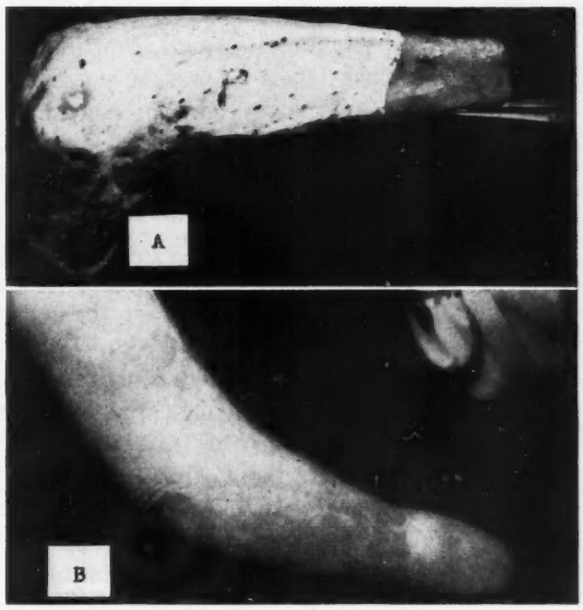

Fig. 6.—(A) Charring of hand and loss of skin of most of the arm from an exploding magnesium flare. (B) Arm covered with dermatome skin grafts and bony stump padded with a pedicle flap prior to fitting with a prosthesis.

Grateful acknowledgment is made of the kindness of Dr. A. L. Wilkie in referring many of these cases and for his continued interest and co-operation.

REFERENCES

1. BUNNELL, S.: Surgery of the Hand, J. B. Lippincott, Philadelphia, 1944.
2. CUTHBERT, J. B.: *Brit. Plastic Surg.*, **1**: 56, 1948.
3. GREELEY, P. W.: *Ann. Surg.*, **124**: 60, 1946.
4. PIERCE, G. W.: *Surg., Gyn. & Obst.*, **45**: 825, 1927.
5. PIERCE, G. W. AND O'CONNOR, G. B.: *Surg., Gyn. & Obst.*, **65**: 523, 1937.
6. YOUNG, F.: *Surgery*, **20**: 117, 1946.

Medical Arts Bldg.

HYPERPOTASSÆMIA AND ELECTROCARDIOGRAPHIC CHANGES IN URÆMIA*

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THE thought that potassium might accumulate within the body and be responsible for some of the "toxic manifestations" of renal disease is not new.[1] A progressive elevation of the serum potassium levels had been observed with some regularity in experimental uræmia, produced by bilateral nephrectomy, bilateral ligation of the ureters and by other means.[2 to 6] In patients with renal insufficiency, however, elevated levels of serum potassium were not consistently observed. In fact, many patients with similar degrees of urea and non-protein nitrogen retention showed normal and even subnormal levels of serum potassium.[7 to 16]

Early investigations were all hampered by the difficulty of doing potassium determinations and by the lack of any other means of identifying potassium effects. In 1938, Winkler, Hoff and Smith[17] clearly demonstrated a regular sequence of electrocardiographic changes which occurred following the intravenous administration of potassium chloride to dogs. These changes were definitely and closely related to concentration of potassium in the serum. The sequence of electrocardiographic events was as follows. The increase in height of the T-wave regularly appeared at potassium concentrations of 5 to 7 mEq/l of serum. The S-T segment depression with diphasic or inverted T-waves appeared at 8 to 10 mEq/l; the P-waves began to disappear at 9 to 11 mEq/l. Finally, disintegration of the entire QRS complex and cardiac arrest occurred at potassium levels of 14 to 16 mEq/l of serum. If the KCl was rapidly injected, ventricular fibrillation resulted.[18, 19] The slow intravenous administration of KCl in rabbits[19] cats[20] and rats[21] has produced similar electrocardiographic changes and elevation of the serum potassium levels.

In 1940, Winternitz *et al.*[22] observed that in dogs made uræmic by bilateral nephrectomy or ligation of the renal arteries, the serum potassium levels taken some time before death were elevated and the corresponding electrocardiographic changes were similar to those described by Winkler, Hoff and Smith.[17] The following year, Hoff, Winkler and Smith[23] demonstrated that dogs rendered anuric by bilateral ureteral ligation or nephrectomy died of cardiac arrest due to potassium intoxication, as proved by the terminal electrocardiograms and by the determinations of serum potassium levels at death.

The earliest observations of the effects of elevated serum potassium levels on the heart in man resulted from the correlation of electrocardiographic changes and the levels of serum potassium following the intravenous administration of KCl[24] or the ingestion of potassium salts[25 to 35] and in other conditions with a disturbed potassium metabolism.[26] The electrocardiographic changes thus obtained were quite similar to those observed in dogs by Winkler, Hoff and Smith[17] but the disintegration of the QRS complexes and cardiac arrest were in most instances associated with a lower range of serum potassium levels.

Electrocardiographic abnormalities were noted in human cases of uræmia long before this relation to elevated serum concentrations was known.[36, 37] These consisted mainly of elevations of the T-wave, and in a few instances the R-wave was decreased along with some elevation of the S-T segment, and in some cases there was a slight widening of the QRS complexes, indicating some degree of intraventricular conduction defect. In recent years, the sequence of electrocardiographic changes characteristic of potasium intoxication terminating in cardiac arrest, similar to those seen in experimental uræmia, have been observed in some cases of uræmia in man associated with spontaneous hyperpotassæmia.[40 to 45] Similar electrocardiographic changes with elevations in the serum potassium levels have also been reported in cases of lower nephron nephrosis.[38, 39]

Although the early electrocardiographic changes, namely elevations of the T-wave, S-T segment depression and absent P-waves associated with varying degrees of spontaneous hyperpotassæmia in human cases of uræmia have been reported with some frequency, there are very few cases recorded in which the

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TABLE I.

Case No.	Diagnosis	Date	Preceding 24 hr. urine vol. c.c.	Time before death	Serum								Electrocardiogram changes				Autopsy findings in heart				
					N.P.N. mgm. %	Creat. mgm. %	CO_2 vol. %	CL. mgm. %	CA. mgm. %	NA. mgm. %	K mgm. %	K. mEq/l	Elevation t-wave	S-T depression	Loss of p-wave	Split Q.R.S.	Weight gm.	Thickness R.V. mm.	Thickness L.V. mm.	Pericardritis	Degree coronary sclerosis (+ to ++++)
1.		Dec. 7	660	96 hrs.	224.0	18.0	32.1	339	—	—	28.3	7.3	+	—	—	—					
H.W.	subacute	Dec. 11	240	40 hrs.	218.5	18.0	—	—	—	—	28.8	7.4	+	—	—	—					
Age 53	glomerulonephritis	Dec. 13 (5:30 a.m.)	160	40 min.	244.5	17.2	—	—	7.3	—	34.2	8.8	+	+	+	±					
M.		Dec. 13 (6:20 a.m.)	160	0	251.5	16.8	32.9	—	7.4	—	34.9	8.9	+	+	+	+	440	6	22	—	+
2.		Jan. 17	1200	22 days	167.5	23.6	27.3	—	—	—	19.3	4.9	—	—	—	—					
G.Z.	Polycystic	Feb. 4	810	4 days	237.5	33.0	22.3	374	6.05	—	29.8	7.6	+	+	—	—					
Age 38	kidneys	Feb. 8	600	50 min.	280.5	—	—	—	—	—	37.2	9.5	+	+	+	±	485	3	18	—	—
M.																					
3.	Carcinoma of bladder	Jan. 17	1000	4 days	339.0	20.8	—	370	—	—	20.2	5.2	—	—	—	—					
G.C.	with obstruction of both	Jan. 19	430	60 hrs.	284.5	25.0	24.8	382	8.75	—	—	—	+	—	—	—					
Age 60	ureters.	Jan. 21	200	1 hr.	312.5	18.5	—	—	—	328	33.2	8.5	+	+	+	±	335	3	16	—	±
F.																					
4.	Extensive tuberculosis	Dec. 29	750	18 days	379.0	16.0	37.8	256	8.2	—	24.0	6.2	+	—	—	—					
M.R.	of kidneys, bladder,	Dec. 30	2980	17 days	288.0	11.0	44.2	274	—	—	16.7	4.3	—	—	—	—					
Age 28	lungs, peritoneum.	Jan. 8	950	8 days	339.0	9.6	—	307	9.2	—	16.2	4.2	—	—	—	—	265	3	12	+	—
M.																					
5.	1. Retroperitoneal neurofibroma.	Oct. 18	43.0	—	112.0	10.9	—	329	8.05	—	24.9	6.4	+	—	—	—					
R.	2. Acute renal failure	Oct. 20*																			
	following injury to	(before)	135.0	—	172.0	17.2	—	335	—	—	26.3	6.7	+	—	—	—					
Age 51	inferior vena cava	Oct. 20**																			
	above renal veins at	(after)	135.0	—	119.0	10.5	40.5	—	—	—	23.7	6.0	+	—	—	—					
F.	operation.	Nov. 10	2800	—	27.0	2.97	—	—	9.65	—	18.9	4.8	—	—	—	—	—	—	—	—	—

*Before treatment with artificial kidney.
**After treatment with artificial kidney.

terminal electrocardiograms and serum potassium determinations were obtained. In three of the cases to be presented here, the electrocardiograms and the serum potassium determinations were obtained within one hour of death.

The purpose of this report is to stress the danger of the toxic effect of elevated serum potassium levels upon the heart in uræmia, as indicated by the electrocardiographic changes, and to report another two fatal cases of uræmia in whom hyperpotassæmia associated with the electrocardiographic changes characteristic of potassium intoxication[17] were found terminally.

Methods.—Electrocardiograms and specimens of blood for chemical analyses were taken at repeated intervals on the 5 patients with uræmia. In Case 1 (Table I) the final electrocardiograms were obtained at the instant of death. In Cases 2 and 3, the electrocardiograms and serum potassium determinations were obtained within one hour of death. In Case 5, the patient recovered and in Case 4, terminal tracings were not recorded.

The electrocardiograms were taken with a "Visocardiette", Sanborn Company, and all tracings were standardized to a deflection of 1 cm. per millivolt.

Results. — From the data summarized in Table I, it can readily be seen that the sequence of electrocardiographic changes and the elevations in the serum potassium levels resembled very closely those found in experimental anuria[23] and in the cases of uræmia with spontaneous hyperpotassæmia observed by others.[38 to 45]

The earliest electrocardiographic abnormality noted was the elevation of the T-wave, which was especially apparent in lead CF_4. The peaked T-waves were not always abnormally increased and in some instances only a slight elevation occurred, which if taken alone without a previous tracing for comparison, were well within normal limits (Case 1, 2 and 3). The T-wave changes became apparent at serum potassium concentrations of 23.7 to 28.8 mgm. % (6.0 to 7.4 mEq/l) (Table I).

With further increase in the serum potassium levels, at concentrations of 28.8 mgm. % (7.4 mEq/l) and above, depression of the S-T segment with diphasic or inverted T-waves were noted. P-waves disappeared at serum potassium levels of 33.2 mgm. % (8.5 mEq/l) and above.

The widening of the QRS complexes, indicating intraventricular block, was observed at serum potassium levels of 33.2 mgm. % and above, and complete disintegration of the entire QRS complex, terminating in cardiac arrest was noted only in the terminal tracing in Case 1, at a serum potassium concentration of 34.9 mgm. % (8.9 mEq/l). In Case 2, however, P-waves were still present and only a moderate degree of intraventricular block was present at a serum potassium level of 37.2 mgm. % (9.5 mEq/l).

From the observations presented in Table I, it is apparent that a severe degree of renal insufficiency as evidenced by the high non-protein nitrogen and creatinine values obtained in the blood was present in all 5 cases. However, there is no correlation between the degree of non-protein nitrogen and creatinine retention in the blood and the serum potassium concentration.

Some degree of acidosis was found in all the cases, as indicated by a reduction in the carbon dioxide combining power of the plasma. Hypochloræmia was present only in Case 4 (Table I). The serum sodium concentration was determined in Case 3 only and it was found to be slightly below normal.

The serum calcium concentration varied from 6.05 to 9.63 mgm. % and none of the patients showed any symptoms or signs of tetany. The biochemical alterations in the serum noted in our patients were in close accord with the observations of others.[33, 41, 42, 47]

Although the elevations in the serum potassium levels were not directly related to the degree of renal insufficiency, as indicated by the elevations in the non-protein nitrogen and creatinine (Table I), there was a close correlation between the potassium retention and the volume of urine excreted. The elevations of serum potassium levels were noted only in the presence of persistent oliguria or almost complete anuria.

The neurological disturbances, consisting of paræsthesia, weakness or flaccid paralysis reported in some cases of hyperpotassæmia[30, 31] were absent in all our cases. In Case 2 (Table I) the patient was comatose for 36 hours prior to death, but in Cases 1, 3 and 4, consciousness persisted up to the very end. In Case 1, respira-

tions continued for 3 minutes after the heart had stopped beating.

Post-mortem examinations were made in Cases 1 to 4 (Table I). At autopsy the hearts weighed from 280 to 480 gm. Acute seropericarditis was present in Case 4, who died of widespread tuberculosis and cachexia. Terminal electrocardiographs were not obtained in this case. In general, the coronary vessels showed very little or no sclerotic changes. Numerous sections taken from the hearts revealed no other pathological abnormalities than the moderate degree of hypertrophy already described in Table I.

DISCUSSION

From the data presented in this study and from the previous observations of others,[33, 34, 38 to 45] it appears evident that potassium metabolism may be disturbed in patients with renal disease. The elevations of serum potassium concentrations and the associated electrocardiographic changes observed in the five uræmic patients described above, were similar to those described in experimental anuria,[22, 23] and in those cases of uræmia with spontaneous hyperpotassæmia in man.[38 to 45]

The importance of persistent oliguria or anuria for the development of hyperpotassæmia has already been stressed.[23, 33, 40, 41, 43, 44] In patients with renal insufficiency, but without oliguria or anuria, the potassium clearance may be reduced,[33] but such individuals are able to excrete the basal quantity of potassium resulting from tissue catabolism.[33, 34] Such patients frequently develop polyuria, and although potassium is excreted at a lower rate, the total amount excreted in 24 hours is sufficient to keep the serum potassium concentration from rising.

However, when an extra amount of potassium must be excreted following the ingestion of KCl salts or of increased potassium in the diet, the diseased kidneys excrete it more slowly and in some instances retention of potassium occurs, causing only slight temporary elevations of serum potassium levels.

In patients with renal insufficiency associated with oliguria or anuria the excretion of potassium is markedly reduced resulting in an increase in the serum potassium concentration. In addition to the diminished urinary excretion, the coexistence of such extra renal factors as dehydration, excess potassium in diet or excessive tissue catabolism may further increase the potassium in the serum.

The danger of giving potassium salts to patients with renal impairment has frequently been stressed,[43 to 47] and several deaths have been reported following the administration of KCl to patients with renal insufficiency.[26, 30, 44] The survival time of anuric dogs has been decreased by the administration of KCl,[23] or by an increase in the dietary intake of potassium.[48]

The results of this present study indicate that even in the presence of severe renal insufficiency, the serum potassium concentration may be normal. Elevations of the serum potassium levels were only seen after the patients had developed a persistent oliguria or anuria (Table I). The hyperpotassæmia may at times be transitory (Cases 4 and 5, Table I), and frequently may not be demonstrable until shortly before death.

The coexistence of a moderate degree of acidosis in Cases 2 and 3, and the dehydration and hypochloræmia due to excessive vomiting in Case 4, may have played some additional rôle in causing an increase in the serum potassium.[31, 33]

The serum potassium levels obtained terminally in Case 1, and those determined shortly before death in Cases 2 and 3 (Table I) associated with the characteristic electrocardiographic changes (Figs. 1 to 4), were somewhat lower than those reported in terminal uræmia in dogs,[23] but were comparable to the values found in man.[31, 40, 41, 44, 47] Thus far, the critical lethal level in man has varied between 8.1 and 10.5 mEq/l of serum, but cases surviving 12.27 mEq/l and 14.1 mEq/l have been described.[29, 49]

Gross and microscopic findings of the hearts in our cases support the views that there is no evidence of the existence of a specific uræmic myocarditis[42] and that electrocardiographic changes of hyperpotassæmia are not correlated with the size of the heart or the degree of coronary sclerosis.[45] The increase of serum potassium produces a functional rather than anatomical alteration in the heart muscle.

The diagnosis of potassium intoxication, therefore, depends on the demonstration of an elevation of the serum potassium concentration associated with the characteristic sequence of electrocardiographic changes. These findings may not be apparent until shortly before death (Cases 1 to 3; Figs. 1 to 4).

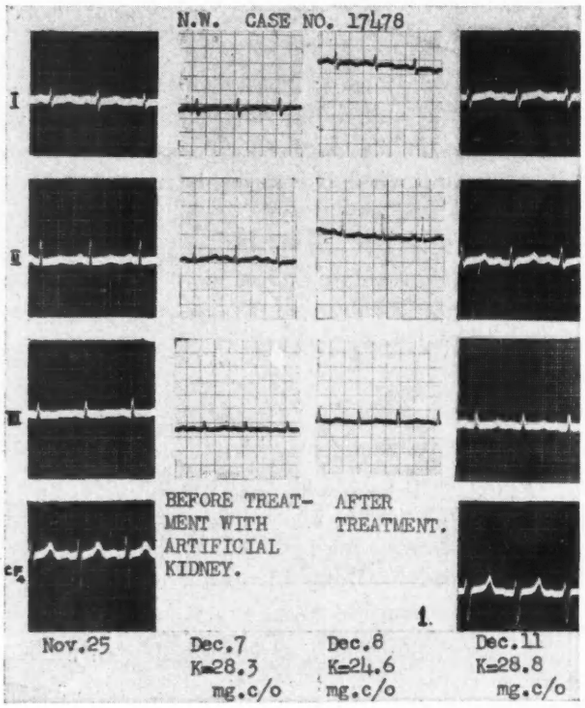

Fig. 1. (Case 1).—Note that although the serum potassium levels were elevated, slight elevations of the T-wave can be seen in tracing of December 11, 1949, as compared to previous tracings, but by themselves are not sufficiently prominent so as to be diagnostic of hyperpotassæmia.

Although the electrocardiographic changes have been found to be fairly characteristic of potassium intoxication[17] and were closely related to elevations of serum potassium levels, the range of serum potassium concentrations within which these changes occurred has been found to vary considerably. The earliest signs

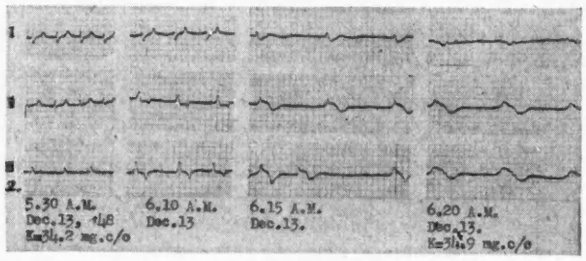

Fig. 2. (Case 1).—Further tracings taken at the time of death clearly show the sequence of electrocardiographic as seen in hyperpotassæmia. Note the high T-waves; depression of the S-T segment with the diphasic or inverted T-waves; the absence of P-waves and the disintegration of the QRS complexes.

of hyperpotassæmia, the elevation of the T-waves, occurred at serum potassium levels between 23.7 and 24.9 mgm. % (6.0 to 6.4 mEq/l) in Cases 4 and 5 (Figs. 4 and 5), whereas in Case 1, the toxic effects were not visible until the serum potassium concentra-

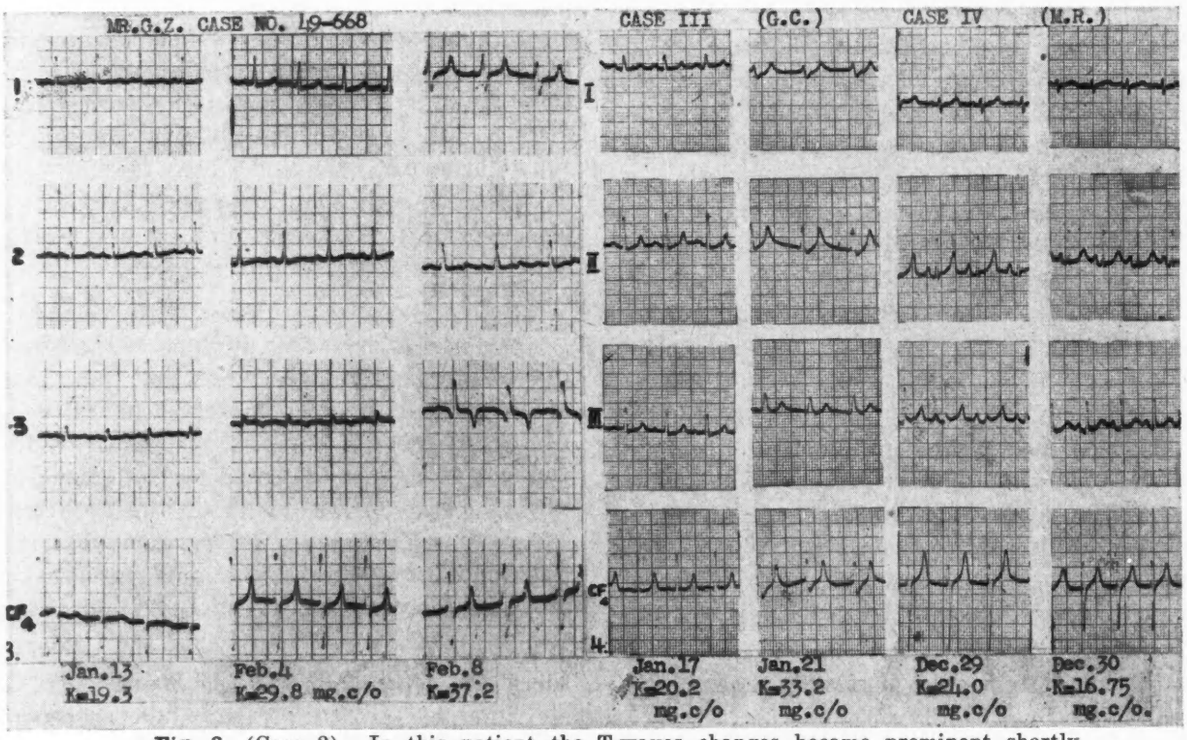

Fig. 3. (Case 2).—In this patient the T-waves changes became prominent shortly before death, at a level of serum potassium of 37.2 mgm. % (9.5 mEq/l). **Fig. 4.** (Case 3).—The tracing taken on January 21, 1949, one hour before death shows high T-waves, absence of the P-waves and early splitting of the QRS complexes. **Fig. 4.** (Case 4).—Note the reduction in amplitude of the T-waves with the return of the serum potassium level to normal.

tion had risen above 28.3 mgm. % (7.4 mEq/l) (Figs. 1 and 2). Complete disintegration of the QRS complex and cardiac arrest occurred at a level of 34.9 mgm. % (8.9 mEq/l) in Case 1 (Figs. 1 and 2) but in Case 2, (Fig. 3) P-waves were still present and only a moderate degree of intraventricular block was seen at a serum potassium level of 37.2 mgm. % (9.5 mEq/l). These observations are in close agreement with the results of previous investigators.[31, 34, 47]

From the data presented here and from the experimental and clinical observations of others,[23, 33, 40, 41, 42, 44, 47] it has not been possible to account for the individual variations in the serum potassium concentrations and the degree of electrocardiographic changes. Darrow *et al.*[50] found no correlation between the degree of the electrocardiographic changes and the concentration of potassium in the cardiac muscle. In patients with uræmia and hyperpotassæmia, it may be possible that the coexisting disturbances of water and electrolyte metabolism, particularly the concentration of serum sodium, calcium and hydrogen ions, may influence the individual cardiac response to an elevation of the serum potassium level.[51, 53] Further study, however, is required before the significance of these disturbances can be ascertained.

The administration of sodium chloride,[31] insulin,[38] calcium,[29, 31, 38, 44, 45, 51, 52] hypertonic glucose,[29, 38] and the adrenocortical compounds[54, 57] have been employed in the treatment of potassium intoxication. The use of sodium chloride has been of value in patients with salt depletion, where the latter may have contributed to the development of renal failure and potassium intoxication.[31] This is well illustrated in Case 4, (Table I), in which the intravenous administration of 2,000 c.c. of 5% glucose in normal saline produced a marked diuresis and lowered the serum potassium from 24.0 to 16.75 mgm. % in less than 24 hours (Fig. 4).

The injection of hypertonic glucose and insulin, by causing a shift of the potassium from the extracellular to the intracellular compartments associated with the deposition of glycogen may be of some value in lowering the serum potassium below the critical level.[29, 38] Thus far, the administration of calcium has exerted only a temporary antagonist effect on

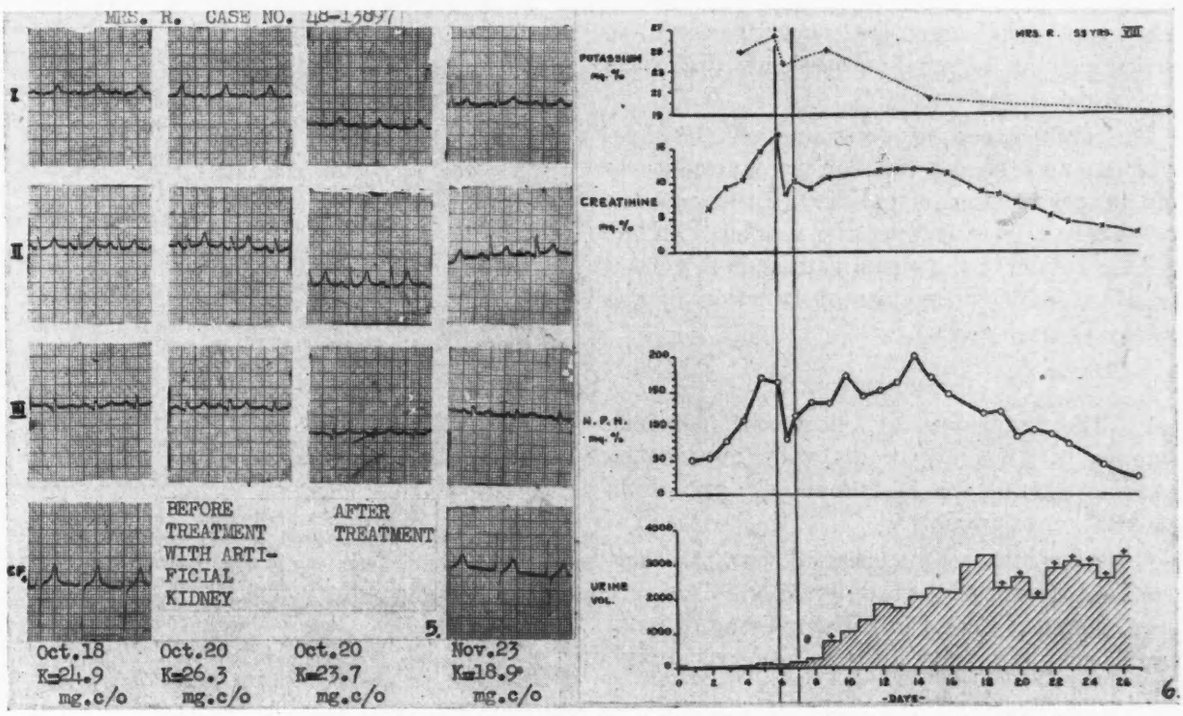

Fig. 5.—Note the reduction in amplitude of the T-wave after treatment with the artificial kidney. On the November 23 record, the appearance of a normal tracing coincided with improvement in renal function. **Fig. 6.**—This illustration clearly shows the marked lowering of the serum potassium level to normal with increase in urinary excretion. Note the slight lowering of the serum potassium concentration during treatment with the artificial kidney on 6th day.

the heart by increasing the irritability of the ventricular muscle.

In general the treatment of hyperpotassæmia should be directed toward the regulation of water and electrolyte disturbances which frequently accompany the uræmia. The over-enthusiastic administration of intravenous fluids frequently leads to death due to pulmonary œdema.[39] A sound physiological therapeutic regimen for the treatment of patients with anuria or oliguria in lower-nephrosis has recently been described by Strauss.[39]

Recently, during treatment with the artificial kidney, by markedly reducing the KCl content of the dialysing fluid, it has been possible to lower the serum potassium levels by removing potassium from the body.[55] In Case 1, 7.6 grams of potassium was removed from the body by artificial dialysis, but following this treatment the marked oliguria persisted and the potassium reaccumulated in sufficient amount to lead to cardiac arrest from hyperpotassæmia 6 days later (Figs. 1 and 2).

The results of this present study are in agreement with the observations of others,[33, 40 to 47] that elevations of serum potassium levels with the characteristic sequence of electrocardiographic changes, as seen in potassium intoxication in animals[17] are more commonly found in patients dying of renal insufficiency than have hitherto been recognized.

The toxic effects of potassium on the myocardium may be reversible if recognized early and proper treatment applied.[29] In Case 5, the patient was treated with the artificial kidney and the return of the serum potassium to normal coincided with the return of function of the kidney (Figs. 5 and 6).

CONCLUSIONS

1. The sequence of electrocardiographic changes in uræmic patients with hyperpotassæmia is similar to that found in potassium intoxication in animals.[17]

2. Hyperpotassæmia associated with the characteristic electrocardiographic abnormalities are more commonly found in patients dying of renal insufficiency than have hitherto been recognized.

3. The importance of persistent oliguria or anuria and extrarenal factors in the development of hyperpotassæmia has been discussed.

4. The toxic effects of potassium on the myocardium may be reversible, if the hyperpotassæmia is recognized early and proper treatment applied.

REFERENCES

1. VOIT, C.: *Ztschr. f. Biol.*, 4: 77, 1868.
2. NOGUCHI, I.: *Arch. f. exper. Path. u. Pharmakol.*, 108: 73, 1925.
3. BECKMANN, K., BASS, E., DURR, R. AND DROSIHN, G.: *Ztschr. f. d. ges. exper. Med.*, 51: 333, 1926.
4. HARTWICH, A. AND HESSEL, G.: *Klin. Wchnschr.*, 7: 67, 1928.
5. NICHOLSON, W. M. AND SCHECHTER, A. J.: *Bull. Johns Hopkins Hosp.*, 60: 346, 1937.
6. BOLLIGER, A. AND BREH, F.: *Zentralbl. f. inn Med.*, 49: 825, 1928.
7. MEYERS, V. C. AND SHORT, J. J.: *J. Biol. Chem.*, 48: 83, 1921.
8. ZONDEK, H., PETOW, H. AND SIEBERT, W.: *Klin. Wchnschr.*, 1: 2172, 1922.
9. WILKINS, L. AND KRAMER, B.: *Arch. Int. Med.*, 31: 916, 1923.
10. NELKEN, L. AND STEINITZ, H.: *Ztschr. f. klin. Med.*, 103: 317, 1926.
11. RABINOWITCH, I. M.: *J. Biol. Chem.*, 62: 667, 1925.
12. ATCHLEY, D. W., LOEB, R. F., BENEDICT, E. M. AND PALMER, W. W.: *Arch. Int. Med.*, 31: 611, 1923.
13. SALVESEN, H. A.: *Acta. med. Scandinav.*, 69: 126, 1928.
14. GREEN, C. H., WAKEFIELD, E. G., POWER, M. H. AND KEITH, N. M.: *Biochem. J.*, 26: 1377, 1932.
15. MACULLUM, A. B.: *Am. J. Med. Sc.*, 156: 1, 1918.
16. OLMER, D., PAYAN, L. AND BERTHIER, J.: *Compt. rend. Soc. de Biol.*, 87: 867, 1922.
17. WINKLER, A. W., HOFF, H. E. AND SMITH, P. K.: *Am. J. Physiol.*, 124: 478, 1938.
18. WIGGERS, C. J.: *Am. J. Physiol.*, 93: 197, 1930.
19. NAHUM, L. H. AND HOFF, H. E.: *J. Pharmacol. & Exper. Therapeut.*, 65: 322, 1939.
20. CHAMBERLAIN, F. L., SCUDDER, J. AND ZWEMER, R. L.: *Am. Heart J.*, 18: 458, 1939.
21. WENER, J.: Unpublished data.
22. WINTERNITZ, M. C., MYLON, E., WATERS, L. L. AND KATZENSTEIN, K.: *Yale J. Biol. Med.*, 12: 623, 1940.
23. HOFF, H. E., SMITH, P. K. AND WINKLER, A. W.: *J. Clin. Invest.*, 20: 607, 1941.
24. HARRIS, I. AND LEVIN, D. A.: *J. Physiol.*, 89: 153, 1937.
25. THOMSON, W. A. R.: *Brit. Heart J.*, 1: 269, 1939.
26. *Idem*: *The Lancet*, 1: 808, 1939.
27. STEWART, H. J. AND SMITH, J. J.: *Am. J. Med. Sc.*, 201: 177, 1941.
28. SHARPEY-SCHAFER, E. P.: *Brit. Heart. J.*, 5: 80, 1943.
29. GOVAN, C. D. AND WEISETH, W. M.: *J. Pædiat.*, 28: 350, 1941.
30. FINCH, C. A. AND MARCHAND, J. F.: *Am. J. M. Sc.*, 206: 507, 1943.
31. FINCH, C. A., SAWYER, G. C. AND FLYNN, J. M.: *Am. J. Med.*, 1: 337, 1946.
32. KEITH, N. M., OSTERBERG, A. E. AND BURCHELL, H. B.: *Proc. Mayo Clin.*, 17: 49, 1942.
32. KEITH, N. M., OSTERBERG, A. E. AND BURCHELL, H. B.: *Proc. Mayo Clin.*, 17: 49, 1942.
33. KEITH, N. M., KING, H. E. AND OSTERBERG, A. E.: *Arch. Int. Med.*, 71: 675, 1943.
34. WINKLER, A. W., HOFF, H. E. AND SMITH, P. K.: *J. Clin. Invest.*, 20: 119, 1941.
35. KEITH, N. M., OSTERBERG, A. E. AND BURCHELL, H. B.: *Ann. Int. Med.*, 16: 879, 1942.
36. WOOD, J. E. JR. AND WHITE, P. D.: *Am. J. M. Sc.*, 169: 76, 1925.
37. MISSKE, B.: Cited by Langendorf and Pirani (42).
38. BYWATERS, E. G. L.: *J. Am. M. Ass.*, 124: 1103, 1944.
39. STRAUSS, M. B.: *New England J. Med.*, 239: 683, 1948.
40. MARCHAND, J. F. AND FINCH, C. A.: *Arch. Int. Med.*, 73: 384, 1944.
41. KEITH, N. M., BURCHELL, H. B. AND BAGGENSTOSS, A. H.: *Am. Heart J.*, 27: 817, 1944.
42. LANGENDORF, R. AND PIRANI, C. L.: *Am. Heart J.*, 33: 282, 1947.
43. TARAIL, R.: *Am. Heart J.*, 35: 665, 1948.
44. STEWART, H. J., SHEPHERD, E. M. AND HORGER, E. L.: *Am. Heart J.*, 5: 821, 1948.
45. KEITH, K. M. AND BURCHELL, H. B.: *Am. J. M. Sc.*, 217: 1, 1949.
46. SMILLIE, W. B.: *Arch. Int. Med.*, 16: 330, 1915.
47. TARAIL, R.: *Am. J. Med.*, 5: 828, 1948.
48. ADDIS, T. AND LEW, W.: *J. Clin. Invest.*, 18: 773, 1939.
49. SNAPPER, I.: *J. Am. M. Ass.*, 131: 251, 1946.
50. CRISMON, J. M., CRISMON, C. S., CALABRESI, M. AND DARROW, D. C.: *Am. J. Physiol.*, 139: 667, 1943.
51. WINKLER, A. W., HOFF, H. E. AND SMITH, P. K.: *Am. J. Physiol.*, 127: 430, 1939.
52. WOOD, E. H. AND MOE, G. K.: *Fed. Proc.*, 1: 95, 1942.
53. AMBERG, S. AND HELMOLTZ, H. F.: *J. Pharm. & Exper. Therap.*, 12: 19, 1919.
54. WINKLER, A. W., SMITH, P. K. AND HOFF, H. E.: *J. Clin. Invest.*, 21: 419, 1942.
55. WENER, J. AND DE LEEUW, N. K. M.: *Proc. Soc. Exper. Biol. & Med.*, 71: 18, 1949.
56. WENER, J., DE LEEUW, N. K. M. AND MACLEAN, J. T.: To be published.

THE CYTOLOGICAL DIAGNOSIS OF MALIGNANT CELLS IN VARIOUS BODY FLUIDS

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BECAUSE of the interest in cytological methods for the diagnosis of malignancy, it was felt that it might be of interest to review the results obtained at Shaughnessy Hospital in order to ascertain the accuracy of the methods in use and to determine if possible the usefulness of such procedures.

For the purpose of analysis we have reviewed all the cases in whom pleural fluids, ascitic fluids, sputa or gastric washings have been examined for the presence of neoplastic cells. This comprised a total of 164 specimens from 103 patients during the interval between January, 1946 and June, 1948. Only those cases with a known end result have been included; all those termed "malignant" have shown a related neoplasm at autopsy, while the "non-malignant" cases have either shown no evidence of tumour at autopsy or have been followed for a period of at least eight months since the last cytological examination and are showing no clinical or radiological evidence of neoplasm. It is realized that the numbers of specimens are insufficient for statistical analysis but for convenience sake percentages are given.

TABLE I.
ANALYSIS OF TOTAL CASES

Type	*Number cases*	*Positive cytologic report*	*Negative cytologic report*
Malignant.....	48	32 (68%)	16 (32%)
Non-malignant.....	55	4 (7.2%)	51 (92.8%)
Total.....	103	36 (34.9%)	67 (65.1%)

ANALYSIS OF CASES

From the total of 103 patients a diagnosis of malignant or "suspicious" malignant cells was made on fluids from 36 cases (34.9%). The analysis of the entire group in relation to proved malignancy and non-malignancy is given in Table I.

It will be noted from this analysis that a false positive report was made in 4 of the 55 non-malignant patients, or 7.2%. This compares very favourably with other series reported, *e.g.*, Chapman and Warren,[1] in their recent paper, reported 3 positive cell blocks in 49 patients with no evidence of malignant neoplasm (6%).

Since it appeared to us that the most important feature of such a review would be to determine its accuracy, the series was further analyzed, breaking down the proved malignant and non-malignant groups into the various types of material examined.

MALIGNANT CASES

Table II summarizes the findings reported on the 48 cases in which a malignant neoplasm was proved to be related to the exudate examined for malignant cells.

In the group of proved malignancies cell block examination prior to death revealed malignant cells in 66% of the pleural fluids examined, in 100% of ascitic fluids, in only 20% of gastric washings and 53% of sputa.

We feel that the explanation of the low percentage of positives in the gastric washings is possibly technical. Since cellular detail is quickly lost in gastric fluid due to self digestion, it is most important that gastric washings be carefully collected in formalin and sent to the laboratory immediately. In the past few months, we have increased the number of such examinations from cases of suspected gastric neoplasms but our results are still disappointing and not comparable to the other groups.

With regard to sputum examination we have greatly increased the number of positives by changing our technique from the Schaudin fixed smears to a cell block method described by Hunter and Richardson[2] as outlined later in this paper. In a two year period from Janu-

TABLE II.
ANALYSIS OF PROVED MALIGNANT CASES

	Pleural fl.	*Ascitic fl.*	*Gastric wash.*	*Sputum*	*Total*
Proved malignant cases....	12	14	5	17	48
Malignant cells found.....	8	14	1	9	32
Per cent positive.....	66%	100%	20%	53%	68%

ary, 1946 to December, 1947, only three sputa were reported positive from a total of 9 cases of proved bronchogenic carcinoma (33%), whereas in the six month period January to June, 1948, using the cell block technique, 6 positive reports were made on 8 cases of bronchogenic carcinoma (75%). These figures we feel emphasize the importance of technical details in the cytological examination of exudates for malignant cells.

NON-MALIGNANT CASES

In this series, there were 55 patients in whom autopsy showed no malignant neoplasm or the patients are still living, with no evidence of neoplasm, for a period of at least 8 months following the last cytological examination. The analysis of this group is summarized in Table III.

In the entire series of 164 specimen examinations, false positive or suspicious reports were given in 4; all of which were pleural fluids. These proved to have the following diagnoses; chronic pulmonary fibrosis with recurrent episodes of pleural effusion; myocardial infarction with hydrothorax; arteriosclerotic heart disease with pleural effusion, and idiopathic spontaneous pneumothorax with effusion. This latter case was interesting in that the cells thought to be neoplastic appeared to be columnar and were forming a small acinus. In reviewing this slide, however, it was noted that the cells were regular in size, shape and staining.

It is a well known fact that most false positive reports of malignancy are made on pleural and peritoneal transudates. This is because the shed endothelial cells may continue to proliferate in the fluid, which acts as a culture medium for the cells, resulting in bizarre shapes and forms, mitoses and even pseudo-acinus formation. Obviously it is therefore most important for one to treat such fluids with the utmost conservatism when reporting the presence of malignant cells.

TIME INTERVAL BETWEEN POSITIVE DIAGNOSIS AND DEATH

An analysis of the time interval between a positive diagnosis of malignant cells in the "exudate" examined and the death of the patient has proved disappointing. In all, there were 27 cases in which this interval could be definitely ascertained, the average duration between positive cell diagnosis and death being only 4 months. Table IV summarizes our findings:

It is obvious that the life expectancy in a patient with neoplastic cells in pleural or ascitic fluids will be short; but we were disappointed to find such a short duration of life in patients with positive sputa in bronchogenic carcinoma. Admittedly the number of cases here (7) is far too small to be of any statistical value, however it is our impression that the relatively large number of cases of bronchogenic carcinoma seen at this hospital are too advanced for surgery when positive sputum is found. This is not in agreement with other workers for instance Woolner and Macdonald[3] who feel that search of sputum for positive cells is a very valuable procedure in the early diagnosis of bronchogenic carcinoma. This divergence in views may indicate that our cases are initially seen in a more advanced stage. On the other hand, Woolner and Macdonald have not as yet reported a follow-up of their cases and it is possible that the end results in their series may also prove disappointing.

There is no question in our minds as to the value of this procedure as a diagnostic measure but actually it appears to be more of academic

TABLE III.

ANALYSIS OF NON-MALIGNANT CASES

	Pleural fl.	*Ascitic fl.*	*Gastric wash.*	*Sputum*	*Total*
Non-malignant cases.....	16	3	8	28	55
No tumour cells found.....	12	3	8	28	51
Per cent negative.....	75%	100%	100%	100%	92.8%
Per cent false positive.....	25%	0	0	0	7.2%

TABLE IV.

TIME INTERVAL BETWEEN POSITIVE DIAGNOSIS AND DEATH

Positive diagnosis	*Cases*	*Range in days*	*Average in months*
Pleural fluid.....	7	1–440	4
Ascitic fluid.....	13	2–400	2
Sputum.....	7	15–736*	6

*This case had lobectomy with recurrence.

interest, at least as far as treatment is concerned, in that the finding of tumour cells indicates a very grave prognosis in the majority of cases.

CASE 1

A 40-year old male complained of cough for six months, excess sputum one month and disturbed vision with occasional loss of memory for one month. A provisional diagnosis of carcinoma of cæcum with pulmonary and glandular metastases had been made at another hospital where biopsy of a supraclavicular lymph node had revealed metastatic adenocarcinoma. Radiological examination revealed a diffuse density obscuring the entire right lung field, with mottling of the left chest and probable atelectasis of the right lower lobe; 1,500 c.c. of reddish turbid fluid were removed from the right chest 2 days after admission and histological examination revealed epithelial tumour cells, many of which were forming acini (Fig. 1). Examination of other systems were negative except that the fundi showed temporal

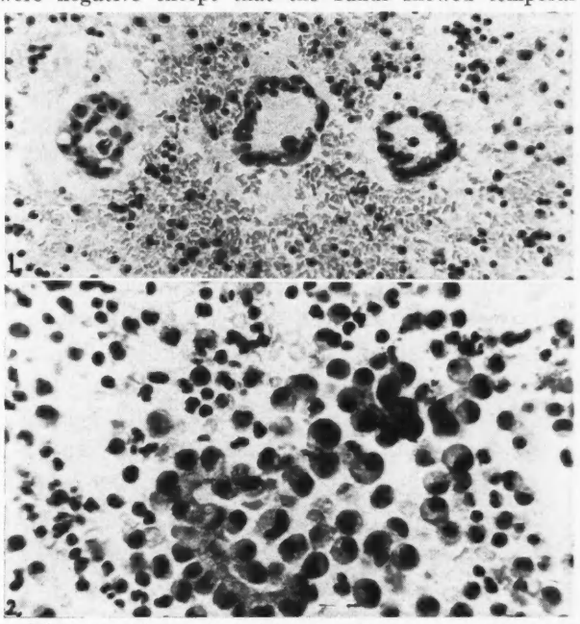

Fig. 1. (Case 1).—Adenocarcinoma of bronchus. Tumour cells forming acini in aspirated pleural fluid. Cell block technique, H. and E. stain. **Fig. 2.** (Case 2).—Primary carcinoma liver. Mass of tumour cells with dark nuclei and attempted acinus formation in aspirated ascitic fluid. Cell block technique, H. and E. stain.

pallor on the right side and indistinct disc margins on the left. He rapidly deteriorated and died 5 months after admission. Autopsy revealed a primary bronchogenic adenocarcinoma with pleural involvement on the right, extension to the left lung and metastases to brain.

CASE 2

A 71-year old male complained of a lump in the upper abdomen, anorexia, post-prandial pain and weakness. He had noted the lump seven months before. Examination revealed ascites, a large mass in right upper quadrant and mild jaundice; 2,000 c.c. of turbid fluid were withdrawn from the abdomen 4 days after admission and histological examination of blocks prepared from the sediment revealed many polymorphonuclear leucocytes and endothelial cells. In addition, there were many larger cells with rich cytoplasm and deep-staining irregular nuclei, some of these were in clusters and in an occasional area, they showed attempted acinus formation (Fig. 2). These were diagnosed as malignant tumour cells. A liver biopsy revealed the presence of an undifferentiated adeno-carcinoma which was thought to originate either from pancreas or possibly the biliary tract. The patient died one month after admission. Autopsy revealed a primary neoplasm of the liver with metastases to ribs and spine; and a portal cirrhosis. Many of the tumour nodules were on the surface and some were ulcerated, leading to hæmorrhage.

CASE 3

A 64-year old male complained of substernal pain of six months' duration, difficulty in swallowing and recent weight loss. Gastro-intestinal investigation had been reported negative six months previously at another hospital. Examination now revealed tenderness in epigastrium with a suggestive mass and evidence of ascites. Tissue blocks from the sediment of gastric washings revealed isolated clusters of irregular epithelial cells with deep-staining, irregular nuclei which were diagnosed as malignant tumour cells (Fig. 3). Radiological exam-

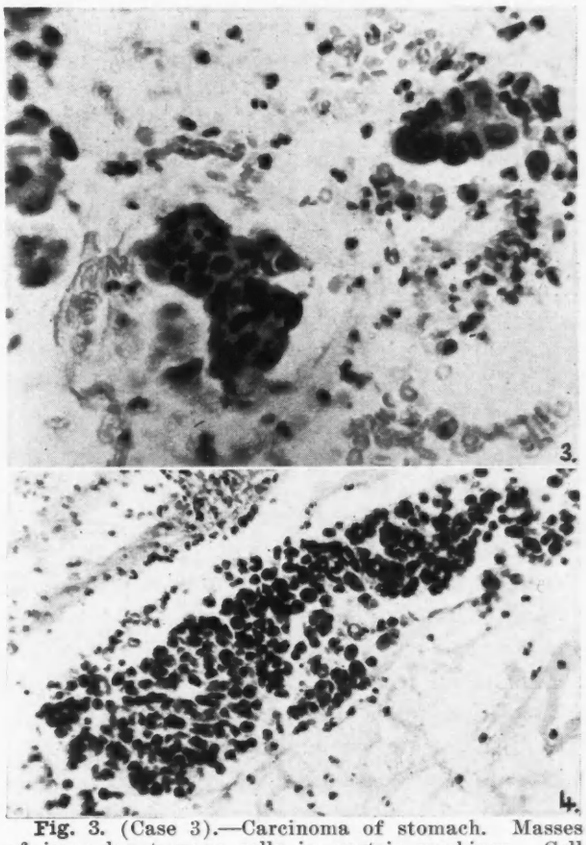

Fig. 3. (Case 3).—Carcinoma of stomach. Masses of irregular tumour cells in gastric washings. Cell block technique, H. and E. stain. **Fig. 4.** (Case 4).—Primary bronchogenic carcinoma, anaplastic small cell type. Large mass of deep staining, hyperchromatic tumour cells in expectorated sputum. Cell block technique, H. and E. stain.

ination now revealed an extensive infiltrating carcinoma involving the proximal two-thirds of the stomach and probable involvement of the lower œsophagus. Two weeks later, ascitic fluid was withdrawn and examination of its sediment also revealed malignant tumour cells. The patient was discharged home as an inoperable gastric carcinoma.

CASE 4

A 67-year old male was admitted with complaints of pain in left chest, weight loss and occasional blood streaked sputum of two months' duration. Radiological examination revealed a marked density in the entire upper half of the left lung, at the periphery was a large cavity with a fluid level and planograms showed multiple small cavities throughout. Bronchoscopy failed to show a tumour and an attempt at needle aspiration was un-

successful. Three sputum examinations for tumour cells proved negative but sections of a block prepared from the 4th sample revealed clusters of small ovoid, hyperchromatic cells embedded in mucus and purulent exudate (Fig. 4). These were diagnosed as malignant tumour cells and were found again in three further specimens. He slowly deteriorated and expired 9 months after admission. Autopsy revealed a primary bronchogenic carcinoma of anaplastic small cell type with metastases to regional lymph nodes, brain, pancreas and adrenals.

METHODS

At the outset most of the examinations were performed on smears prepared from the sediment of fluid, from sputum or gastric washings. These smears were fixed in Schaudin's fluid and stained with hæmatoxylin and eosin. For the past year we have been using the method described by Hunter and Richardson.[2] As noted above, we are obtaining better results by this latter method. It is much easier to search serial sections of blocks of tissue than smears, the neoplastic cells usually stand out clearly and can be spotted with the low power objective. It is absolutely essential that the material be collected as described below and sent to the laboratory immediately, otherwise disintegration of cells takes place rendering recognition impossible.

Fluids.—Aspirated fluids are sent to the laboratory immediately, when one-third volume of 10% formalin is added, or the fluid can be placed in the formalin directly it is obtained. On receipt at the laboratory a quantity of saturated picric acid is added to the specimen. The amount will vary with the quantity of the fluid but we use sufficient to cause a definite flocculation, usually about an equal volume. The precipitate which forms is allowed to settle, the supernatant fluid is poured off and the sediment centrifuged. It will be found that the picric acid has caused the sediment to become firm and with a glass rod this can now be removed as a small ball of tissue which may be placed in lens paper and treated for paraffin embedding. If the sediment in the formalized fluid is heavy, centrifuge this and treat the precipitate with the picric acid instead of as above.

Gastric washings. — The stomach must be empty. If there is gastric retention, aspirate the stomach completely. Introduce about one ounce of normal saline, withdrawing and reinjecting several times. Discharge the last aspiration into an equal volume of 10% formalin. On receipt at the laboratory add approximately an equal volume of saturated picric acid which will increase the precipitate, allow this to stand overnight, pour off the supernatant and centrifuge the sediment using a glass rod to tamp it down.

Sputum—Collect the sample of sputum directly in 10% formalin. Treat as for gastric washings but be careful in adding the picric acid not to obtain too large a quantity of precipitate. In some cases, it may be necessary to centrifuge the specimen when obtained, pour off the supernatant and then add an equal volume of picric acid to the remaining sediment.

Staining.—We have compared results, using hæmatoxylin and eosin and Papanicolaou's method. In our hands we can see no advantage in the latter over a good H. and E. stain. Providing a satisfactory hæmatoxylin stain is used nuclear details are excellent.

CONCLUSIONS

The examination of pleural fluid, ascitic fluid, sputum and gastric washings has proved of diagnostic value in the series of 164 specimens from 103 patients reviewed. In all, positive reports were made in 34.9% of cases. The method was accurate in 92.8% of cases, there being 4 false positive reports in the entire series. These comprised 7.2% of fluids examined from patients eventually shown to have no malignant neoplastic lesion. These results compare favourably with other reported series.

The false positives were confined to pleural fluids. It is emphasized that the utmost conservatism should be maintained in interpreting neoplastic cells in transudates or exudates since endothelial cells proliferating in such a "culture" medium may assume very bizarre shapes and forms.

We recommend the method of cell block preparation as described by Hunter and Richardson[2] in preference to the smear technique. In our hands, we have found the former method to give higher positive results.

The usefulness of this procedure when viewed from the treatment aspect proved disappointing, since the finding of neoplastic cells indicates a very grave prognosis. The average duration of life from the first positive report was only 4 months.

REFERENCES

1. CHAPMAN, C. B. AND WHALEN, E. J.: *New England J. Med.*, 237: 215, 1947.
2. HUNTER, W. C. AND RICHARDSON, H. L.: *Surg., Gyn. & Obst.*, 85: 275, 1947.
3. WOOLNER, L. AND MACDONALD, J.: Mayo Clinic: Personal communication and exhibit American Society of Clinical Pathology, Chicago, 1948.

CASE REPORTS

PERNICIOUS ANÆMIA COMPLICATED BY MYELOGENOUS LEUKÆMIA*

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To those who deal with large numbers of pernicious anæmia patients, the occurrence of concomitant disease is not an unusual finding. The majority of these associated conditions are unrelated etiologically to pernicious anæmia, and they are of interest chiefly on account of the bearing they have on the course of the disease. Less common are leukemoid reactions and changes suggesting leukæmia in the blood of pernicious anæmia patients.

Von Leube in 1900 described a rapid and progressive disorder which was characterized by changes in blood similar to those of pernicious anæmia together with those of myelocytic leukæmia. To these, the name "leukanæmia" was given and there is little justification for the term other than descriptive.

In the morphological study of pernicious anæmia the macrocytosis of the erythrocyte plays such a striking part that relatively little attention is paid the leucocytes, other than to note leukopænia or relative lymphocytosis. However in 1932, Heck[1] reported on the myeloid immaturity in pernicious anæmia, pointing out that leukoblasts or stem cells could be found particularly in cases in which the erythrocytes were below the two million level. In 1939 Sharp[2] reported on the myeloid pattern in pernicious anæmia and stated that myeloid immaturity did occur and often persisted until the red blood elements are restored to a normal level and balance.

Few reports are to be found in which leukæmia was superimposed on a pre-existing pernicious anæmia. Rich and Schiff[3] reported a case in 1936, in which chronic lymphatic leukæmia occurred in a patient with macrocytic anæmia. After the use of liver therapy the macrocytic anæmia responded on two occasions with a rise in the reticulocytes and an increase in the red count and hæmoglobin. In 1941 Sterne *et al.*,[4] reported a case of pernicious anæmia complicated by myelogenous leukæmia.

These cases appear to be true Addisonian anæmia terminating in leukæmia, one chronic lymphatic and the second, in subacute myelogenous leukæmia.

The purpose of this report is to add another case in which true pernicious anæmia existed for ten years, well controlled with liver therapy and terminated with a final picture of acute myelogenous leukæmia.

H.B.H., a 60-year old farmer entered the Montreal General Hospital on May 27, 1938. For ten years prior to admission he had experienced headache and numbness of hands, feet, and legs on occasion. Prior to admission these symptoms had become progressively worse and more constant.

Physical examination at this time revealed moderate pallor of mucous membranes, but little if any icterus. The tongue was atrophic. The mental state was clear. Vibration sense was impaired over the lower extremities and co-ordination of legs inaccurate. The reflexes were hyperactive. Spleen and liver were not palpable. The blood pressure was 90/60.

The laboratory studies revealed absence of free hydrochloric acid in the stomach content even after histamine stimulation. The barium series revealed no carcinoma of the stomach. The macrocytic anæmia was moderate: red blood cells 3,070,000; white blood cells 8,650; Hgb. 68% or 10.6 gm.; cell diameter 8.2 cubic microns. Differential—polymorphonuclears 53%, lymphocytes 37%, eosinophiles 4%, monocytes 6%. The patient was started on known potent liver extract and showed a maximum reticulocyte response of 12.5%. Three months later the blood count was recorded as red blood cells 4,610,000; white blood cells 8,100; Hgb. 90% or 14.04 gm. The cell size was normal and the differential count was also normal. Clinical improvement was satisfactory in all respects. During the course of the next ten years the patient continued on liver extract and remained well, performing his duties about the farm and spending the winter months with his son who was a physician.

In January, 1948, the patient began to notice progressive weakness and dyspnœa. He was admitted to hospital and thoroughly investigated for neoplasm with negative results. He was treated with potent liver extract and showed a belated response but not at the expected rate or degree. Transfusions produced immediate improvement. The bone marrow biopsy at this time revealed hypoplasia. The patient was discharged on both liver extract and folic acid but failed to maintain his blood count and was readmitted on May 24, 1948 for transfusions.

At this time he appeared thin and pale. There was a definite glossitis and changes in both vibration sense and two-point discrimination. His colour was lemon yellow. There were no other significant findings. Repeat blood studies showed similar findings to those of January except in the differential count. Red blood cells 1,650,000; white blood cells 4,750; Hgb. 36% or 5.6 gm.; platelets 50,000; reticulocytes less than 1%; red cell diameter 8.4 cubic microns; red cell volume 18%; m.c.v. 109. Differential — polymorphonuclears 37%; lymphocytes 6%; monocytes 4%; eosinophiles 2%; erythroblasts 5%; normoblasts 45%; megaloblasts 1%. The bone marrow again appeared hypoplastic although there was some slight megaloblastic activity. A leukæmic process was now entertained. After 3,500 c.c. of whole blood in seven separate transfusions of 500 c.c. each, the patient returned home improved.

He was readmitted on August 18, with a similar picture as on the previous admission. The positive clinical findings were again meagre. However, the white blood count increased to 41,000 with 74% myeloblasts and myelocytes. The peroxidase stain revealed 67% positive and 33% negative cells. The condition was diagnosed

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as acute myelogenous leukæmia. The patient was discharged home after six transfusions of whole blood. He died on October 14.

Post mortem examination approximately 12 hours after death revealed a spleen weighing 500 gm., firm and rubbery and reddish brown in colour with a grayish tint. There were a number of perisplenic hæmorrhages. The liver was markedly enlarged (1,770 gm.). The organ was of the same colour and consistency as the spleen. The lymph nodes were grossly normal. The sections of bone marrow were reddish brown with a grayish tint and appeared soft and hyperplastic.

Microscopically there was evidence of myeloblastic and myelocytic metaplasia of the bone marrow, spleen, liver, and lymph nodes, mediastinal, para-aortic, and mesenteric. There were myeloid infiltrations in the kidneys, thyroid, diaphragm, and retro-peritoneal adipose tissue, as well as perisplenic hæmorrhages with leukæmic infiltration of adherent omentum.

The associated conditions found were of no significance.

CONCLUSIONS

This patient represents a case of primary pernicious anæmia, in whom the development of leukæmia was undoubtedly coincidental. Such a case is not to be confused with those cases of leukæmia, usually of the acute type, which in their early development resemble patients with pernicious anæmia. Such cases have sometimes been referred to as leukanæmia but this term has more virtue as a descriptive one than as a diagnostic entity.

REFERENCES

1. HECK, F. J.: *Am. J. Clin. Pathol.*, **2**: 443, 1932.
2. SHARP, E. A. *et al.*: *Am. J. Clin. Pathol.*, **9**: 189, 1939.
3. RICH, M. L. AND SCHIFF, L.: *Ann. Int. Med.*, **10**: 252, 1936.
4. STERNE, E. H. JR. *et al.*: *Am. J. M. Sc.*, **202**: 167, 1941.

PSEUDOCYST OF THE PANCREAS

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"So uncommon is the occurrence of pancreatic cyst", states Mousseau in a recent paper, "that each new case should be worthy of report." It was, therefore, thought advisable to publish a case of pancreatic cyst which came under the observation of the author, several years ago.

Mrs. W.T., born in 1917, was seen by me on October 31, 1941, at Provost, Alberta. Her complaints were: steady pain in the epigastrium, radiating to the left; vomiting for two weeks, throughout the day, which did not give relief. Fat and eggs gave indigestion.

Previous history: no complaints. She had two children, 16 months and three months of age.

Physical examination showed quite pronounced tenderness in the left, upper abdominal region, just above the umbilicus. Otherwise the findings were normal.

The patient was admitted to Provost Municipal Hospital. For the first three days she had severe pain which required morphine, and she vomited large amounts of undigested food. Her temperature was on no occasion higher than 99.8. Urine culture showed no organisms and no growth. The patient was discharged on November 8th, under the diagnosis of cholecystitis. She returned again on November 24, complaining of vomiting for the past two days. There was considerable abdominal tenderness. A mass was felt in the upper abdomen, more towards the left, and it was thought to be due to an inflammatory omentum tumour caused by cholecystitis. The white blood cell count was 10,900. Hæmoglobin 75%. The patient was again hospitalized.

Her complaints of severe pain and vomiting persisted and, after consultation with Dr. F. L. Eid of Macklin, Sask., it was decided to operate under the diagnosis of acute cholecystitis. X-ray facilities were at this time not available in Provost and the patient refused transportation elsewhere. The operation was performed by Dr. F. L. Eid on December 6, 1941. A large mass was found behind the stomach, extending and fitting into the minor curvature of the stomach, retro-peritoneally. The gall bladder was normal. The cyst was drained through a small incision into the hepato-gastric ligament and a large amount of straw-coloured fluid was obtained. A diagnosis of chronic pancreatitis with cyst formation was made. There was profuse oozing which made any further surgical interference impossible. Gauze and a rubber drain were inserted and the abdomen was closed again.

Examination of the fluid at the Provincial Laboratory of the University of Alberta showed presence of a large number of polymorphonuclear leucocytes. There were no tumour cells present. The culture showed *B. coli communis* and a few non-hæmolytic streptococci. Diastase was present in the fluid. There was a large amount of serous discharge from the drainage, which became purulent on December 10. The patient's temperature, which was 102 on admission and which had fallen to normal by December 1, rose steeply postoperatively to 102.6. Sulfathiazole therapy was started and the temperature fell again and settled down again to normal by December 17. The discharge, which was at first profuse, diminished about December 12 and the patient was discharged with her operative wound discharging very little.

On January 18, 1942, she presented herself with severe upper abdominal pain, especially in the right side, and vomiting. Her condition cleared up quickly under sedation, but it was decided to refer her to the University of Alberta Hospital at Edmonton for further investigation.

On February 18, 1942, an exploratory laparotomy was performed by Dr. R. Anderson at the University of Alberta Hospital and it was found that the stomach was adherent over the distal third to the old Kocher incision. It seemed unwise to release these adhesions because of their firmness and because of the mobility of the rest of the stomach, excepting a portion of the lesser curvature which was firmly adherent to the pancreas. Examination of the pancreas revealed a fairly normal head but an area about two inches wide over the body was indurated and firmly adherent to the stomach. The mass in this part of the pancreas did not appear to be cystic in nature but gave the impression of resolving, acute inflammation. No further operative interference was done and the patient progressed very favourably after her operation.

On January 3, 1947, she was delivered of a normal baby in an uncomplicated delivery and stated at that time that she had not had any further complications whatsoever. She was again contacted lately, and in a letter dated January 17, 1949, she states that she has had no further complaints with the exception of a "gall-bladder" attack last August, which subsided quickly. She claimed to feel very well otherwise.

The case reported here bears out the facts which Mousseau and Kling so aptly laid down in their paper. We were dealing, undoubtedly, with pseudocyst formation according to the classification of Robson and Cammidge as modi-

fied by Mousseau and Kling. Had x-ray equipment been available to us at that time, it might have been possible to have arrived at the correct diagnosis preoperatively. It would be advisable to keep the possibility of a pancreatic cyst in mind in cases of upper abdominal complaints of rather obscure etiology.

Sincere acknowledgment to Dr. R. Anderson of Edmonton, for supplying me with the operative report of this patient.

REFERENCE

1. MOUSSEAU, L. P. AND KLING, S.: *Canad. M. A. J.*, 59: 550, 1948.

CLINICAL and LABORATORY NOTES

NEVER TRANSFUSE A WOMAN WITH HER HUSBAND'S BLOOD*

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Never transfuse a woman with her husband's blood? Not if they are of the same blood group and the same Rh type? No, not even then, except in the direst emergency or if the woman can no longer bear children. By transfusing her with her husband's blood though it be of the same blood group and the same apparent Rh type you may produce fatal erythroblastosis in later fetuses. The following is a case in point:

Mr. R. is Group O, Rh positive. Mrs. R. is Group O, Rh positive.

Pregnancies: 1942, normal boy, O, Rh positive; 1943, normal girl, O, Rh positive.

Mother received a transfusion from her husband and one from another O, Rh positive donor.

1946, male, macerated fetus at 5 months.

1948, male, Group O, Rh positive, at term, with erythroblastosis fetalis of the generalized œdema type. Microscopic study confirmed the diagnosis.

Here then was a case in which husband and wife and diseased baby,—and also the second donor—all appeared to be of the same blood group so far as both the A-B-O and Rh systems were concerned and yet fatal erythroblastosis had developed. What was the explanation?

Dr. Robert Tanner, who attended the woman in her 1948 confinement, kindly obtained permission for us to do the autopsy on the baby and every facility in investigating the family. The following immediate observations were made:

1. The baby's red cells gave a strong positive Coombs' reaction[1] indicative of the attachment to them of an immune antibody.

2. The mother's serum contained an antibody that agglutinated the red cells of both the husband and the baby, indicating that she had been sensitized to a factor or factors contained in these cells.

It was, therefore, evident that the O, Rh positive blood of the mother differed significantly from the O, Rh positive blood of her husband and her baby, to the extent that both were antigenic for the mother. In searching for the difference we did not need consider the A-B-O system. The difference had to lie in the Rh system or in some other system.

On the basis of probability the Rh system was first investigated. The Rh positive blood factor is known to exist in several forms which are serologically distinguishable and separately antigenic. It was found that, while the Rh type of the father did in fact differ from that of the mother, yet the mother's and baby's Rh type was identical. Since they were identical the antibody in the mother's blood that clumped the baby's cells could not be one that reacted on any factor in the Rh system. This system was thus ruled out.

In conversation with Dr. R. R. Race of the Lister Institute, London, he suggested the probability that the antibody was anti-Kell which he and his associate[2] first reported in 1946, but it was not until Dr. Ruth Sanger, recently associated with Race, visited our laboratory, that this identification was proved.

I need not go into details here: the exact specificity of the antibody and the inheritance in the family of the blood factor—the Kell factor—that gave rise to it, will be reported elsewhere. The points I would make are these:

1. In addition to the A-B-O and Rh blood factor there are others, which we cannot examine for routinely, and which can and do occasionally produce maternal sensitization in exactly the same way as does the Rh factor.

2. The one way of making certain that a woman will be sensitized to *any* unusual blood factor, whether Rh or other, that a future fetus may inherit is to transfuse her with her husband's blood.

It is our experience, as it has been of others, that about 20% of pregnant Rh-negative women with Rh antibodies in their blood have had a previous transfusion, most of which have been given subsequent to marriage. The need for transfusion in them is rarely so great that time cannot be taken (*a*) to be certain of the Rh status of donor and recipient so that no Rh-negative woman receive Rh-positive blood and (*b*) to find a donor other than the husband for the woman. At least 20% of the cases of erythroblastosis can be prevented if these simple precautions are taken.

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REFERENCES

1. COOMBS, R. R. A., MOURANT, A. E. AND RACE, R. R.: *Brit. J. Exp. Path.*, 26: 255, 1945.
2. *Idem*: *The Lancet*, 1: 264, 1946.

THE CANADIAN MEDICAL ASSOCIATION

Editorial Offices—3640 University Street, Montreal

(Information regarding contributions and advertising will be found on the second page following the reading material.)

EDITORIAL

THE IMPORTANCE OF NUTRITION

IN the more primitive stages of society there may be an instinctive knowledge of what to eat. But in the complexity of modern civilization nutrition becomes a more difficult problem. Instinct is no guide in choosing food whose virtue has been processed to an æsthetically pleasing sterility; and instinct fights a losing battle against wrongly interpreted or even incomplete scientific investigation. There is no likelihood of a return to mere instinctive choice of food. Rather is the science of nutrition developing more and more rapidly. But it is interesting to see that in thus developing there is a tendency to go back to the principles which underlay the instinctive process. The history of this development has been impressively traced for us in the Frank Billings Lecture by Dr. J. S. McLester.* He shows that the foundations of our knowledge of metabolism were well laid by Lavoisier's conception that life was a chemical process. Then followed the work of such pioneers as Liebig and Lusk. This generation of workers discovered that the law of conservation of energy is applicable to nutrition, with all the implications of that fact. To them it seemed that the exchange of energy was the chief consideration, and calories were given first place.

Then came a period in which dietary needs were sacrificed to methods of treatment; the starvation treatment of typhoid fever is the outstanding example. The handling of peptic ulcer at first was also based on a starvation regimen, until the Lenhartz and then the Sippy diets came in, and even they were inadequate. In a later stage the idea of economizing on protein took root apart from the field of disease. The conception of intestinal auto-intoxication from protein decomposition was blindly accepted in the early part of the century (and possibly is not yet quite discredited), and to accentuate this, Chittenden's experiments on low protein diet, on himself, led many away from the right path. As Dr. McLester shows, Chittenden's experiments suffered both from lack of control groups (a flaw still found in much research work) and from allowing insufficient time for judging the effects of prolonged low protein diet. There were also incorrect conclusions from experimental work, that high protein diet was damaging to the kidneys.

The discovery of the vitamins of course was the most dramatic of all the developments in our knowledge of nutrition. It produced a wave of enthusiasm which has not even yet properly levelled off to its proper dimensions, although, by constant repetition it is probable that the recognition of the sufficiency of a well balanced diet is becoming more general.

Without forgetting these things which are behind us, we are now pressing forward in what Dr. McLester calls the protein era. In ordinary growth, above all, in pregnancy, as well as in disease, the part played by protein is coming to be recognized in all its tremendous proportions. The resistance to infection is based on the rôle of protein in antibody formation. The antibody globulins of the blood are simply normal serum globulins, which have been specifically altered, and their adequate production depends on sufficient intake of amino acids.

Medical and surgical treatment is gradually coming to allow nutrition its proper place. But perhaps it is too soon to claim that protein has quite come into its own. It is safe to say that far too many internists and teachers of medicine do not realize the value of good nutrition; or, if they do, they do not apply it. Dieticians and nutrition experts have their place in special dietary regimens. But the medical practitioner should be perfectly capable of seeing that the all-important general nutrition of his patients is maintained. Usually this does not call for special technical knowledge so much as those two valuable qualities, commonsense and diligence.

* J. S. McLester: Protein Comes into Its Own, *J. Am. M. Ass.*, **139**: 837, 1949.

Erratum

In the recent article by Dr. J. H. MacDermot on "Food and Medicinal Plants Used by the Indians of B.C." reference was made to work done on devil's club for the treatment of diabetes, and the credit for this was inadvertently given to Dr. G. E. Darby of Bella Coola. The work actually was done by Dr. R. G. Large of Prince Rupert.

EDITORIAL COMMENT

The Diabetic Association of Ontario

The formation of the Diabetic Association of Ontario is a valuable and practical step in dealing with the problem of diabetes. The actual treatment of the disease will still remain in the hands of the physician, but there are many problems connected with diabetics which are not strictly medical and yet call for solution; such, for instance, as camps where diabetic children can be dealt with; boarding houses where diabetics can obtain meals as specially needed; education of employers with regard to employing diabetics; the promotion of plans for early detection of diabetes; to carry on the publicity required for the various objects of the Association.

These are a few of the objectives before this newly formed association, which owes its existence largely to the stimulation of Dr. C. H. Best. Physicians can aid greatly by advising their diabetic patients to join. Not the least advantage of such a group is that it can give its weight in directing projects for the betterment of the diabetic population. Similar organizations of course exist on both sides of the Atlantic, and it is to be hoped that Dr. Best's praiseworthy efforts will result in yet wider growth. Further information regarding the Diabetic Association of Ontario may be obtained from Mrs. J. H. Byrne, Assistant Secretary-Treasurer, Diabetic Association of Ontario, 621 Jarvis Street, Toronto.

MEDICAL SOCIETIES

Canadian Neurological Society

The first annual meeting of the Canadian Neurological Society was held in Montreal, Quebec, May 20-21, 1949, under the presidency of Dr. Wilder Penfield. Scientific sessions were at the Montreal Neurological Institute, McGill University, and at the University of Montreal. An excellent neurological program and a large attendance ensured an initial success for the new Society.

The inaugural dinner was held at Le Cercle Universitaire de Montreal. Here the bilingual atmosphere and the fresh association of Canadians drawn together by their common interest in the neurobiological sciences gave strength to the remarks of Dr. Penfield who, in his Presidential address,* observed that a society is a body of companions and he hoped that this companionship would broaden into common friendships.

At the business session it was decided to hold the 1950 meeting in Halifax at about the time of the C.M.A. meeting there. The following new officers were elected: *President*—Dr. J. C. Richardson, Toronto; *Vice-president*—Dr. Frank Turnbull, Vancouver; *Secretary-Treasurer*—Dr. Allan Walters, Toronto.

* "Neurology in Canada and the Osler Centennial": *Canad. M. A. J.*, **61**: 69, 1949.

Canadian Association of Pathologists

On June 15, 1949, representative pathologists from Alberta, Saskatchewan, Ontario, New Brunswick, and Newfoundland, including Dean Lindsay, Saskatoon; Dr. D. F. Moore, Saskatoon; Dr. John Adams, Saskatoon; Dr. N. G. B. McLetchie, Regina; Dr. Lynn, Regina; Dr. John J. Ower, Edmonton; Dr. R. C. Riley, Calgary; Dr. Lola McLetchie, Calgary; Dr. John Duffin, Calgary; Dr. L. Whitaker, St. Catharines; Dr. J. Hamilton, Kingston; Dr. R. A. H. McKeen, Saint John; Dr. J. R. Josephson, St. John's, met in the Board Room of the University of Saskatchewan to form a Canadian Association of Pathologists. This association was formed as a direct result of the increasing problems of the pathologist in his relationship to the rest of the medical profession as well as the hospitals and other agencies by which he is employed. Those present expressed their grave dissatisfaction with present conditions in the field of pathology as a whole. A tentative slate of officers was elected including an eastern vice-president, Dr. M. Simon, Montreal, and a western vice-president, Dr. D. F. Moore, Saskatoon, as well as a secretary-treasurer, Dr. John Hamilton, Kingston, and ten regional representatives: Dr. H. Taylor, Vancouver; Dr. J. Duffin, Calgary; Dr. N. G. B. McLetchie, Regina; Dr. J. M. Lederman, Manitoba; Dr. L. Whitaker, St. Catharines; Dr. C. Auger, Quebec; Dr. R. A. H. MacKeen, Saint John; Dr. O. C. MacIntosh, Antigonish; Dr. H. Shaw, Charlottetown; Dr. J. E. Josephson, St. John's.

Canadian Ophthalmological Society

The twelfth annual meeting of the Canadian Ophthalmological Society was held at Jasper Park Lodge, Jasper, Alberta, June 17 and 18, 1949. Dr. Jules Brault of Montreal was Chairman. There was a very excellent attendance and the scientific program was of a high quality. The following officers were chosen for the 1949-50 period: *Past President*—Dr. Jules Brault, Montreal; *President*—Dr. R. F. Nicholls, Edmonton; *Vice-president*—Dr. G. Stuart Ramsey, Montreal; *Secretary*—Dr. J. F. A. Johnston, Toronto; *Treasurer*—Dr. A. E. MacDonald, Toronto; *Council*—Dr. Henri Pichette, Quebec; Dr. M. R. Levey, Edmonton; Dr. Norman L. Elvin, Winnipeg; Dr. R. T. Hayes, Saint John; and Dr. John A. McLean, Vancouver. The next meeting is to be held in Digby Pines, Digby, Nova Scotia, on June 22, 23 and 24, 1950.

CANADIAN ARMED FORCES

News of the Medical Services

The Naval Medical Service has had a very active summer. Seventeen medical officers of the Reserve have taken naval training ashore and afloat to date and more are expected before the year closes. Thirty-three veteran medical students and 64 surgeon cadets of the University Naval Training Division have also taken training in naval hospitals and afloat. The average training period for the medical officers has been two to six weeks, while veteran and U.N.T.D. medical students were in training from early June to the first week in September.

At present Surgeon Lieutenant Nelson B. Reilly, R.C.N.(R) of Ottawa, Ontario, is serving afloat and will have the opportunity of studying the medical aspect of cold environment ashore and afloat as far north as River Clyde on Baffin Island.

It is anticipated that at least twelve more medical officers, R.C.N.(R) will be attending the course in medical aspects of Special Weapons and Radioactive Isotopes commencing this fall in the U.S. Naval National Medical Centre, Bethesda, Maryland.

Colonel K. A. Hunter, O.B.E., R.C.A.M.C., has resumed his appointment as Command Medical Officer at Central

Command Headquarters, Oakville, Ontario, following his attendance during the past year at the National Defence College at Kingston, Ontario. Lt.-Col. R. J. Nodwell, O.B.E., R.C.A.M.C., acting Command Medical Officer during Colonel Hunter's absence, has been posted to Vancouver, B.C., as Area Medical Officer, British Columbia Area.

Colonel R. A. Gordon, R.C.A.M.C., of Toronto, Ont., has been appointed A.D.M.S. Central Command Section Medical Advisory Staff.

Fifteen Active and Reserve Force R.C.A.M.C. Officers attended the 10th course on the Medical Aspects of Atomic Explosion at the U.S. Army Medical Centre, Washington, D.C., held from September 19 to 23.

Lieutenant General Sir Neil Cantlie, C.B., M.C., F.R.C.S., K.H.P., M.B., Director General of Army Medical Services for the British Army will be in Canada during the first week of November of this year. During this time General Cantlie will visit Army Headquarters and it is proposed will also visit certain R.C.A.M.C. establishments. General Cantlie while in North America will be attending the XII International Congress of Military Medicine and Pharmacy, Mexico City, Mexico, October 23 to 29, 1949, and the Annual Convention of the Association of Military Surgeons of the U.S.A., Washington, D.C., November 10, 11 and 12, 1949, as well as making an extensive tour of U.S. Service medical facilities.

Air Marshal P. C. Livingston, C.B., C.B.E., A.F.C., F.R.C.S., Director General Medical Services, Royal Air Force, arrived in Canada by British Overseas Airways Corporation, August 27, 1949. Air Marshall Livingston is making a liaison visit to the R.C.A.F. which will further correlate the development of aviation medical aspects of R.A.F. and R.C.A.F. Accompanied by Group Captain A. A. G. Corbet, Director of Health Services, R.C.A.F., the Air Marshal visited Air Force medical installations at Montreal, Winnipeg, Edmonton, Vancouver and the Institute of Aviation Medicine, Toronto. At the R.C.A.F. units he outlined by lecture "The Preparation and Purpose of Parachute Medical Teams in the R.A.F.". In addition to his Canadian tour, Air Marshall Livingston attended the Aero Medical Association meeting in New York City and paid liaison visits to the U.S. Forces.

The Director and Assistant Director of Health Services (Air) and three other R.C.A.F. Medical Officers along with the Medical Director General, R.C.N. and a representativve of D.G.M.S. (Army) also attended the meeting.

CORRESPONDENCE

The Family Planning Association

To the Editor:

This Secretariat, which was set up at the end of last year, is receiving an increasing number of enquiries from all parts of the world from women needing medical advice on birth control. It would be of great assistance to me if any medical practitioners who are prepared to give such advice would communicate with me so that I can put them in touch with the patients. I would also be glad to give further information on the work of the Secretariat, and any technical advice required to any doctor who cares to write to me.

I should also be glad if any doctor who is visiting Great Britain would like to see the work of our Clinics here would communicate with this office, 64 Sloane St., London, S.W.1, so that I can arrange for visits.

HELEN COHEN,
International Secretary,
The Family Planning Association.

Gold Salts in Arthritis

To the Editor:

After reading Dr. Dean Robinson's paper on rheumatoid arthritis (August, 1949), we feel that it is a duty to congratulate him for his splendid work and brief exposé. Although we do approve mostly every detail, we could not help wonder why regarding his treatment, he has chosen "Lauron", among all other gold preparations. We would have been glad if Dr. Robinson had supplied us with more reasons for his choice.

Gold thioglucoanilide (Lauron) is an organic gold compound that is almost insoluble (one in 20,000,000 parts of water), suspended in oil to prolong absorption. Accordingly, it is of slow absorption. In fact, it appears in the plasma two weeks after injection, while soluble salts (myocrysine, solganal) take six to eight hours. It constitutes a "depot therapy". X-ray of buttocks after four years shows deposit of gold at the site of the injection and traces of the salt are found in the blood. This leads to the conclusion that with lauron we have a continuous flow of gold and therefore continued improvement. As for its toxicity, lauron is advertised as a low toxic compound, lower than any other available, and according to clinical investigations conducted by Dr. Sabin of Cincinnati, it is non-toxic in mice and reactions are very rare and slight.

The opinion of Dr. Richard H. Freyberg, (Comroe Arthritis, 4th Edition, 1949), is quite different and we quote: "Reports of therapeutic effectiveness and lower tolerance of gold thioglucoanilide (Lauron) seem to be not so advantageous as they would at first appear. Animal and human studies have shown that larger amounts of insoluble salts injected in oil remain for long periods unabsorbed. In order to be therapeutically effective, gold must be absorbed in solution. The effectiveness of such a drug, therefore, depends on the small amount that is absorbed from the total amount injected. The fact that the inert majority of the insoluble salt can amount to a dose many times larger than the amount usually employed when a soluble gold salt is used, seems to be of no advantage, and it may be disadvantageous from the standpoint of toxic potentialities. Reports, thus far, include no cases of lethal toxicity from parenchymatous organ or blood disease. It seems quite clear with our present knowledge that all insoluble salts have less advantage than disadvantage as therapeutic agents in humans. It is more reasonable to expect improvements in gold compounds to come from the development of preparations which will be more readily and uniformly absorbed, circulated, and excreted rather than substances that are insoluble and that are absorbed and eliminated very slowly."

Later on he added: "Toxicity from gold may occur at any time following the first injection of gold salt throughout the course of treatment and for several months after treatment has been discontinued; also all gold salts that may have therapeutic value have toxic potentialities. And all insoluble gold salts reactions have been very unpredictable, chiefly because absorption varies so greatly. It is mostly this disadvantage which militates against their use." . . . . "For treatment of humans, therefore, it seems at this time wise to select a soluble gold salt to be injected intramuscularly. Thus, a soluble compound that can be injected intramuscularly appears to be the type of gold preparation to be preferred."

In citing contradictory opinions of renowned authors, we hope to have shed some light on this product and, therefore, helped others in making their own decision regarding lauron.

LEOPOLD MANTHA, M.D.
LUCILE JULIEN, M.D.

Hôpital Général, Ottawa.

SPECIAL CORRESPONDENCE

The London Letter

(From our own correspondent)

The Health of the Nation

The Registrar-General's Review of England and Wales for the period, 1940-45, provides some interesting data on the trend of mortality rates during the war years. The number of deaths registered during this period was 3,078,550, of which 60,342 were caused by enemy action. The standardized death rate fell from 9.8 per 1,000 living in 1938 to 9.0 in 1945 for males and from 7.4 to 6.4 for females. The deaths of centenarians were 111 males and 520 females, and the age of one of the males was reputed to be 112. Deaths attributed to alcoholism fell from 144 in 1940 to 26 in 1945. At ages 40 to 45 cancer accounted for 20% of deaths, compared with 15% in 1931-33. The effect of immunization on diphtheria is strikingly illustrated by the fact that in the age-period 1 to 5 years the risk to the immunized child of dying from diphtheria is one-thirtieth of the risk to the non-immunized child. The number of deaths from diphtheria fell from 2,480 in 1940 to 722 in 1945. A disturbing feature of the report is the marked increase in deaths due to violence, other than operations of war, in children, principally as a result of road accidents. In boys the increase was due mainly to motor accidents and drowning, whilst in girls it was due to motor accidents and burns. In each year covered by the report accidents accounted for more deaths than any other causes in boys at ages 10 to 15.

The report for 1947 of the Chief Medical Officer to the Minister of Health, which has also just been published, indicates that in spite of austerity conditions the general health of the nation remains satisfactory. Thus, the infant mortality rate has fallen to 41 per 1,000 live births, and the maternal mortality rate has fallen from its 1946 level of 1.43 in 1,000 total births to 1.17. Three disturbing features that will require careful consideration are: (*a*) an increase of 3% over 1946 in the total deaths from tuberculosis; (*b*) a slight but definite decline in the weight of school children; (*c*) an increase in the number of outbreaks of food poisoning from 422 in 1945 to 765.

M.R.C.P.

The Royal College of Physicians of London has just accepted the report of a committee which it appointed a year ago "to consider whether the examination for the M.R.C.P. as regulated and conducted in the past can meet the needs of the future, and to make recommendations". The major part of the report is devoted to detailed consideration of the methods of conducting the examination, and most of its recommendations are intended to ease the strain both on examiners and candidates without in any way lowering the standard demanded. The two important recommendations are that "membership of the college should signify a knowledge of general medicine that justifies further training as a consultant" and "the examination should be taken early in training, normally about two years after qualification". The adoption of these recommendations indicates a definite change in policy, as hitherto the membership of the college has always been taken to indicate consultant status. Now, apparently, it is only an indication that the holder of it is considered a suitable candidate for consultant status. That the importance of this change of policy is appreciated by the college is indicated by the fact that the whole subject is to be reviewed again within two years.

The Old and Infirm

The recent publication in the *British Medical Journal* of the Lumleian lectures, on "Problems of Ageing and Chronic Sickness", delivered before the Royal College of Physicians by Professor A. P. Thomson, has focussed attention once again on a problem which is attaining increasing urgency in the modern state. Professor Thomson's thesis, in brief, is that the segregation of the aged sick in special hospitals is to be deprecated. Many of the inmates of such institutions are not really "sick", and to confine them in hospital is harmful to them both physically and mentally. In addition it is wasteful of nursing staff, already dangerously short in this country. The proper place for the care of the aged and infirm is at home or in special hostels, and they should only be admitted to hospital when they develop a medical or surgical condition that requires active treatment.

Poliomyelitis and Trains

The present outbreak of poliomyelitis, which, fortunately, has not attained the proportions of the epidemic of 1947, has brought up once again the possibility of infection being spread by the contents of the lavatories of railway trains being delivered directly on to the track. The Medical Officer of Health for Southampton has reported that in his area in both 1947 and this year the outbreaks of poliomyelitis have occurred in areas traversed by railway lines. Although the Railway Executive have issued a statement that their "medical advisers are satisfied that there is not the danger that is alleged", there is a general feeling that the whole subject of sanitation on railway trains in this country requires careful review. Recent personal experience on main-line trains certainly indicates that the standard of cleanliness in train lavatories leaves much to be desired.

WILLIAM A. R. THOMSON

London, September, 1949.

ABSTRACTS FROM CURRENT LITERATURE

Medicine

Urinary Obstruction Due to Tripelennamine Hydrochloride. Wolfson, S. A.: *J. Am. M. Ass.*, **140:** 958, 1949.

One of the less frequent side reactions from the use of tripelennamine hydrochloride (pyribenzamine hydrochloride) has been urinary burning and frequency, although there has been no report of actual urinary difficulty. In the course of investigation of the pharmacologic properties of this drug it has been found that it acted as a spasmogenic agent and contracted the duodenum and uterus. In the case reported by the author such an effect on the vesical sphincter could account for the urinary disturbance. The patient was a man in whom cardiospasm due to this drug had been observed, and when the patient suffered from an allergic skin eruption, and was given, in addition to a vaccine, 50 mgm. tablets of pyribenzamine 4 times daily urinary disturbance developed within 24 hours. The disturbance consisted of a painless obstruction, only a dribbling stream being possible. Examination of the prostate and external genitalia revealed essentially normal conditions; urinalysis and the determination of residual urine in the bladder were normal. The symptoms abated by the morning following discontinuance of the drug. Two months later, when the vaccine had been discontinued, and during which period urinary function had remained normal, 50 mgm. of the drug were administered as a test at 7 a.m. and repeated at noon. By 4 p.m. the urinary difficulty returned, but no more drug having been given it had subsided by the following morning.

D. E. H. CLEVELAND

Studies of the Human Colon: 1. Variations in Concentration of Lysozyme with Life Situation and Emotional State. Grace, W. J., Seton, P. H., Wolf, S. and Wolff, H. G.: *Am. J. M. Sc.*, **217:** 241, 1949.

Lysozyme a bacteriolytic and mucolytic enzyme was first described by Sir Andrew Fleming in 1922, occurring in tears, since when it has been shown to be present in many of the body secretions and notably in the secretions of the small and large bowel. The precise function of this enzyme in the body tissues is not known, as a substrate has not been found for it. Following the observation that lysozyme is high in the gastric juice of patients with peptic ulcer and in the stools of patients with chronic ulcerative colitis these authors have followed its concentration in the stools of normal people and of people suffering from various gastro-intestinal abnormalities paying particular attention to what changes might follow emotional disturbances in these subjects. As well as the stool studies, two of the patients investigated had previously had abdominal operations which had resulted in the external exposure of portions of the intestinal mucosa and the lysozyme content of the mucus scraped from the surface of these exposed portions was examined. The effect of applying lysozyme to the surface of the mucosa of the colon was also studied.

In two subjects who were prone to develop diarrhœa under conditions of anxiety it was noted that the lysozyme content of their stools rose during periods of tension. The patients with ulcerative colitis when subjected to emotional stress and strain and particularly when this inner turmoil was concealed by an outward appearance of calm showed a rapid rise of the enzyme and to quite considerable heights. A similar finding was discovered in six patients studied with mild mucous colitis. A patient with carcinoma of the colon showed normal lysozyme content of the stool. If the experiment in which lysozyme as contained in tears was applied directly to the surface of exposed mucous membrane of large bowel there resulted, following a twenty-four hour exposure, a sharply circumscribed area of inflammation at the site of application; control applications of normal saline and of boiled tears and of dry cotton did not produce a comparable response.

The authors point out that the lysozyme content of the stool is not higher in patients with ulcerative than non-ulcerative lesions of the bowel and they suggest that the enzyme if it is effective in producing destruction of mucous membrane is a precursor to that event rather than its accompaniment or by-product. They conclude that high lysozyme concentration in bowel secretions is an accompaniment of emotional stress and strain and that this increase is particularly great in subjects who are suffering from ulcerative colitis. It is their belief that the concentration of the enzyme rises to higher levels in individuals who conceal their internal emotional stresses.

G. A. COPPING

Tentative Appraisal of Vitamin B_{12} as a Therapeutic Agent. Spies, T. D. *et al.*: *J. Am. M. Ass.*, **139:** 521, 1949.

Vitamin B_{12} per unit of weight, is the most effective antianæmic substance known. It has been found to produce a hæmatologic response in persons who have pernicious anæmia, nutritional macrocytic anæmia and tropical sprue. It is the only pure chemical substance known to be effective in relieving subacute combined degeneration in persons with pernicious anæmia. When vitamin B_{12} is administered to suitable patients, under controlled conditions, reticulocytosis occurs and is followed by an increase in red blood cells, platelets and hæmoglobin. A striking clinical response parallels the hæmopoietic response. About the time the reticulocytes begin to rise, the patients volunteer that they feel stronger. Those whose appetites have failed have a sudden desire for food. Symptoms arising from subacute degeneration of the spinal cord in persons with pernicious anæmia are benefited by the administration of vitamin B_{12}. The severe glossitis present in some cases of macrocytic anæmia heals spectacularly. In patients with sprue and nutritional macrocytic anæmia there is a decrease in the number of stools and a tendency for the stools to return to normal.

The dosage of vitamin B_{12} varies greatly from patient to patient. They observed a slight effect following the injection of as little as 4 micrograms and complete failure on as much as 10 micrograms. A response has occurred in every case when several times these amounts were administered. Perhaps the average patient will respond maximally to 100 micrograms or less. Most patients seem to respond minimally to from 8 to 10 micrograms. Vitamin B_{12} has no effect on the leukopenia of infections or the idiosyncrasies due to drugs, idiopathic purpura, secondary anæmias, aplastic anæmia or leukæmia.

In the management of any of these syndromes of macrocytic anæmia which respond to specific therapy, they followed these five principles: (1) Make a positive diagnosis early in the course of the disease. (2) Institute persistent and intensive therapy promptly. (3) Prescribe an amount of the therapeutic agent in excess of that just necessary to maintain the patient's blood at a normal level. (4) Prescribe a diet rich in animal proteins. (5) Treat promptly all coexisting diseases and any complicating factors.

J. PRESTON ROBB

Diagnosis and Treatment of Lung Tumour. Adams, R.: *Am. Rev. Tuberc.*, **59:** 353, 1949.

The content of this paper is limited to the practical diagnosis and treatment of lung tumour, based on the author's experience with one group of 157 consecutive microscopically proved cases. Pulmonary carcinoma accounts for between 6 and 8% of all cancer cases. The three most valuable approaches to early diagnosis are: (1) education of the public to consult a physician for any cough of over two weeks' duration; (2) education of the profession to inquire for symptoms, to fluoroscope every new patient and to advise roentgenograms when indicated; (3) stop the practice of symptomatic treatment of cough and pleurisy without evaluation of the cause.

The symptoms are early and are so ordinary that they are likely to be disregarded by both patient and physician. The author discusses the incidence and significance of cough, pain, sputum, hæmoptysis and wheezing. Later symptoms are dyspnœa, pleural effusion, severe pain, hoarseness, loss of weight and weakness. Physical signs are related solely to bronchial obstruction or to extension of the growth. The most direct primary evidence is the radiographic demonstration of a tumour mass, of atelectasis or of infection secondary to bronchial obstruction. Bronchoscopy is the next most important diagnostic procedure and is indicated whenever there are findings suggesting bronchial obstruction. If handled by a seasoned endoscopist, 90% of the cases bronchoscoped will have the diagnosis established or stated as a positive suspicion. Examination of the sputum for cancer cells is of value if the test is positive and performed by experienced observers. Other methods of investigation are thoracentesis, thoracoscopy, punch biopsy and thoracotomy. At present, pulmonary resection offers the only hope for cure. For certain lesions lobectomy may be as satisfactory and less hazardous than pneumonectomy, but, for the majority of cases the latter is preferred. The hospital mortality rate for pulmonary resection is 5% with a resectability rate of 31.8%. Resected cases have a 64% chance of being alive and well one year later and a 23% chance five years later. The predominant factor affecting survival time is the cell type; other factors are significant but not determinative.

J. F. SIMPSON

Incipient Pulmonary Tuberculosis in Persons Over Forty. Chaves, A. D.: *Am. Rev. Tuberc.*, **59:** 469, 1949.

There is widespread clinical misconception that pulmonary tuberculosis rarely occurs after the age of thirty. Phthisiologists are aware, however, that incipient pulmonary tuberculosis after forty is not at

all a rarity today and is much more common than is generally supposed. A higher percentage of early tuberculosis in the older age group is being found in various chest clinics throughout the country. During the last few decades there has been a marked change in the epidemiological picture of the disease, with a striking shift of the mortality peak toward the older age group. In 1900 only about 25% of all tuberculosis deaths occurred after the age of 45. At present 50% of all tuberculosis deaths in the United States occur after the age of 45.

The patients in this study were "contacts", had recent "normal" chest films and developed roentgenographic evidence of tuberculosis after their fortieth birthday. Tuberculin testing had not been done on any of the patients prior to diagnosis. The great majority had developed disease within one year of a normal roentgenogram. There were many cases associated with other diseases, especially diabetes, hypertension and arteriosclerosis. The findings in this small selected group indicated that the lesion showed the same tendency to progression as in younger age groups. The most striking finding at the conclusion of the period of observation was the extreme seriousness of the disease. The presence of other diseases was undoubtedly a factor in the poor prognosis.

Theoretically, late incipient pulmonary tuberculosis may be due to: (1) reactivation of old radiologically undetectable foci; (2) new exogenous infection in individuals with a clinically healed primary complex; (3) new exogenous infection in individuals with an obsolete primary infection; (4) recently acquired first infection. The pathogenesis of pulmonary tuberculosis in older people might be less obscure if there were data on the incidence of negative tuberculin reactors in older age groups and of the type of reaction prior to the initial demonstration of pulmonary tuberculosis. The need for such a study is obvious.

J. F. SIMPSON

Early Neurosyphilis. Kopp, I.: *New England J. Med.*, **239:** 1021, 1948.

Invasion of the central nervous system occurs in nearly all cases of syphilis within the first year although it is usually asymptomatic and can only be detected by spinal fluid examination. This incidence of neurological involvement is greatly reduced by the use of penicillin in the treatment of early syphilis. Regardless of the type of treatment employed in early syphilis the spinal fluid should be re-examined four years or more after the primary lesion. A negative examination at this time is good assurance against the future development of neurosyphilis. While penicillin is of great benefit in the therapy of neurosyphilis of the asymptomatic, meningovascular and meningitic types further experience will be required to determine its value as the sole treatment for parenchymatous neurosyphilis. NORMAN S. SKINNER

The Effect of Subacute Bacterial Endocarditis on the Course of the Underlying Heart Disease. Rapoport, B. and Ellis, L. B.: *New England J. Med.*, **239:** 951, 1948.

Chemotherapy may cure subacute bacterial endocarditis in a high proportion of cases but pre-existing cardiac damage is often added to by the occurrence of valvular distortion from the scarring associated with the healing process. Valve cusps and chordæ tendineæ may be ruptured and myocardial fibrosis may be the late result in areas of acute myocarditis, usually subsequent to small infarcts from minute emboli. Fifteen cases of subacute bacterial endocarditis, caused by alpha hæmolytic streptococci, were reviewed after a minimal period of two years after cure of the infection. Four had died, three showing persistence of infection, death in the fourth case being the result of coronary embolism. The remaining eleven patients were well and in four there had been a decrease in heart size. Three cases presented signs (auricular fibrillation, increased dyspnœa, deterioration of the electrocardiogram respectively) suggesting an advancement of cardiac damage. NORMAN S. SKINNER

Surgery

Carcinoma Cells in Sputum and Bronchial Secretions. Woolner, L. B. and McDonald, J. R.: *Surg., Gyn. & Obst.*, **88:** 273, 1949.

Out of 1,600 patients from whom sputum or bronchial secretion wet smears were examined, 150 were reported positive for carcinoma cells. The characteristics of both normal and atypical cells seen in such preparations are described. In 146 cases the source of the malignant cells was believed to be a tumour of the bronchus. In 2 cases the cells were from an œsophageal carcinoma with a tracheœsophageal fistula. There was one case of carcinoma of the trachea and one of the larynx. False positives were given in 3 cases in the series, but it is stated that errors are the result of inexperience of the examiner.

The technique of collecting and staining the specimens is described and the shortcomings of the method discussed. Of the 24 cases in which the bronchogenic carcinoma could be removed, carcinoma cells in the sputum or bronchial secretions provided the only microscopic evidence of cancer in 9. BURNS PLEWES

Management of Compound Facial Injuries. Brown, J. B. and Fryer, M. P.: *Am. J. Surg.*, **76:** 625, 1948.

Some rules for the care of wounds and compound fractures of the face emphasize principles which are fundamental in surgery generally. A complete physical and neurological examination with x-rays of the skull if there has been a period of unconsciousness (proving brain injury) and often of the cervical spine, should precede operation. The primary repair should be done as soon as the patient's general condition permits, preferably within the first 20 hours. Bone fragment replacement may have to await subsidence of swelling. Nerve block with basal anæsthesia is most satisfactory, for the endotracheal method is necessary for general anæsthesia. Cleansing by soap and water, ether and saline is recommended, not antiseptics. Oil and glass must be completely removed. Debridement must be very sparing. Skin edges and bone fragments must be conserved. Buried white silk is recommended for retention sutures. Surface sutures should not extend more than 1 or 2 mm. from the wound edges to avoid permanent scars. Rubber band drains, fine mesh grease gauze, and firm mechanic's waste pressure dressings are recommended.

Displacement of the frontal processes of the maxilla means displacement of the inner canthus and must be corrected early. The problems of antral, zygomatic and mandibular fractures are discussed. The Risdon arch is recommended as in interdental wiring. The general rule is to replace fragments and maintain them with the least manipulation possible. If the final adjustment of bone and soft tissue is not satisfactory, one should not be reticent about re-opening the wound and re-suturing it. BURNS PLEWES

The Surgical Management of Ulcerative Colitis. Miller, G. G., Ripstein, C. B. and Tabah, E. J.: *Surg., Gyn. & Obst.*, **88:** 351, 1949.

As colon surgery has become safer, and the dangers of leaving the diseased colon of ulcerative colitis behind are recognized, simple ileostomy no longer seems an adequate surgical treatment. Colectomy is only indicated in the intractable complicated cases so that a comparison of results in medically versus surgically treated patients is unfair. The acute fulminating type of ulcerative colitis can only be treated surgically if the operation is performed before the patient is moribund. Most surgical cases are from the chronic type of moderate severity where, because of intractability, impending

perforation, stricture formation, polyposis, carcinoma, massive hæmorrhage, abscess and fistula, or segmental ulcerative colitis, operative interference is necessary. Preoperative preparation must aim at the control of cramps and diarrhœa, nutritional deficiencies (negative nitrogen balance, vitamin deficiencies, anæmias, dehydration) and the control of infection. A permanent ileostomy is the price of a good result. The technique used at the Royal Victoria Hospital is described, as is the postoperative care with the use of streptomycin and penicillin. The rectum must be removed whenever there is severe ulceration, stricture, polyps or anorectal fistulas.

BURNS PLEWES

Treatment of Paraplegia Resulting from Trauma to the Spinal Cord. Freeman, L. W.: *J. Am. M. Ass.*, **140:** 949, 1949.

This is a special article based on personal observation on more than 720 cases. It would be impossible to briefly summarize it. The essentials in the care of the patient suffering from paralysis of the legs resulting from injury of the spinal cord are given: (1) Rotation or flexion of the spine should be studiously avoided or the spinal cord may be severed. (2) The deformity of the spine should be promptly reduced by traction or hyperextension or both. (3) The patient must be turned every two hours at least. (4) Proper care of the bladder includes: (*a*) avoidance of distension or continuous contraction; (*b*) encouragement of the development of an automatic bladder; (*c*) avoidance of urinary sepsis, or prompt treatment if it occurs; (*d*) prevention of urinary calculi by exercising upper extremities in bed and by early ambulation. (5) Proper care of the skin: (*a*) avoid prolonged pressure; turn frequently; (*b*) the bed should be clean, dry, smooth and flat; (*c*) maintain adequate protein intake; (*d*) large decubitus ulcers should be repaired surgically. (6) Care of the bowels: (*a*) relieve intestinal distension and constipation promptly, with: (1) pituitrin or neostigmine, (2) enemas and rectal tube; (*b*) watch for and remove fæcal impactions promptly; (*c*) develop proper bowel habits. (7) Watch for, prevent and, if necessary, promptly treat anæmias, hypoproteinæmia and vitamin deficiencies. (8) Constantly be on the alert for complicating emotional reactions and help the patient to accept the reality of his difficulty.

This article is well worth the careful attention of anyone interested in the care of the paraplegic and should be consulted in the original.

PRESTON ROBB

Obstetrics and Gynæcology

Anæmia Simulating Pre-eclamptic Toxæmia. Scott, J. M. and Govan, A. D. T.: *J. Obst. & Gyn. Brit. Emp.*, **56:** 28, 1949.

Thirteen cases of anæmia simulating pre-eclamptic toxæmia are described. Investigations demonstrated the existence of a distinct syndrome, showing the cardinal features of toxæmia, *viz.*, œdema, hypertension and albuminuria. Although the patients were severely anæmic the general symptoms and signs commonly associated with anæmia were absent except in 4 cases, where the anæmic condition was extreme (hæmoglobin less than 5.1 gm. %). Antenatally the syndrome can be distinguished from that of true toxæmia by careful examination of the blood-pressure urine and blood-picture. The true diagnosis becomes apparent after admission to hospital, when changes occur in the blood pressure and albuminuria. The increase in blood pressure is mainly on the systolic side and there is consequent increase in the pulse pressure.

P. J. KEARNS

A Review of a Series of 100 Cases of Vesicovaginal Fistulæ. Krishnan, R. G.: *J. Obst. & Gyn. Brit. Emp.*, **56:** 27, 1949.

One hundred cases of vesicovaginal fistulæ which came under the author's care during 20 months (January, 1945 to April, 1948) are reviewed. They are classified according to their size as large, small, and pin-hole. There were 31 cases of large, 61 cases of small, and 8 cases of pin-hole fistulæ. They are also classified according to their situation as juxta-urethral, mid-vaginal, juxta-cervical, and combined. There were 45 cases of juxta-urethral, 21 cases of mid-vaginal, 21 cases of juxta-cervical, and combined. There were 45 cases of juxta-cervical, and 13 cases of combined fistulæ.

The other pathological changes met with in these cases, such as prolapse of the mucous membrane of the bladder through the fistulous opening, destruction of urethra, severance of the urethra from the neck of the bladder, blockage of the urethral opening at its proximal end, visibility of the urethral opening at the edge of the fistula, destruction of the vaginal portion of the cervix, burial of the vaginal portion of the cervix under the vaginal mucous membrane, adhesions of the fistula to the cervix and pubic arch, and contraction of the lumen of the vagina are described.

P. J. KEARNS

Natural Childbirth in a Teaching Clinic. Thomas, H.: *J. Obst. & Gyn. Brit. Emp.*, **56:** 20, 1949.

Labours are classified as "excellent" when the patient has not asked for or appeared to need anæsthesia or analgesia. Labours are classified as "good' if the patient has had, at some time during the labour, a minimal amount of analgesic or anæsthetic. Minimal here means a single dose of an analgesic and/or nitrous oxide with the contractions at the end of the second stage. These patients are fully conscious at delivery. Labours are classified as "fair" if the patient appeared to have derived some benefit from the indoctrination, but needed a greater amount of analgesia and anæsthesia than the "good" group. Labours are classified as "poor" if the patient seemed to receive no benefit from the technique and required the conventional amount of analgesia and anæsthesia.

P. J. KEARNS

Management of Chronic Endocervicitis in Infertility. Krohn, L., Harris, J. M., Priver, M. S. and Fenmore, M. S.: *Am. J. Obst. & Gyn.*, **57:** 774, 1949.

Abortion, both spontaneous and induced, is an important factor in the etiology of chronic endocervicitis and sterility. Penicillin-oil-beeswax administered intramuscularly is almost a specific form of therapy in the treatment of chronic endocervicitis. With the disappearance of the infection, there is a return of normal sperm migration in the endocervical secretions. The use of penicillin-oil-beeswax is a valuable therapeutic agent in the management of the sterility problem.

ROSS MITCHELL

Roentgen Diagnosis of Adenomyosis Uteri. Goldberger, M. A., Marshak, R. H. and Hermel, M.: *Am. J. Obst. & Gyn.*, **57:** 563, 1949.

Hysterography is of great help in determining the presence of intrauterine pathology. Adenomyosis uteri can be occasionally diagnosed by hysterography, especially when the dye enters the endometrial pits which have invaded the uterine musculature. The above findings have been seen more frequently since the use of skiodan acacia. Hysterography has been very helpful in the institution of more specific therapy. There have been no reactions or ill-effects from the use of skiodan acacia in these cases.

ROSS MITCHELL

The Use of the Male Leopard Frog (Rana Pipiens) as a Pregnancy Test Animal. Brody, H.: *Am. J. Obst. & Gyn.*, **57:** 581, 1949.

The successful use of the male common leopard frog (Rana pipiens) in a test for pregnancy as described by Wiltherger and Miller, and Robbins and Parker is confirmed. A modification of the method is described. This modification eliminates the killing of numerous frogs by "toxic" urines, which was early found a serious drawback to the performance of the test as originally described. The test is reliable (no false positives), although some false negatives were found. The test may be used in summer as well as winter months, though it

may prove necessary to use more frogs for each test in the summer, to allow for individual variation in reactivity. The test is inexpensive, and is sufficiently rapid to be of great value in clinical emergencies, as originally predicted by Robbins and Parker. It is sufficiently simple so that it may be used even in the smallest laboratories without special equipment or provision for the care of animals. ROSS MITCHELL

Dermatology

Cutaneous Granuloma from Accidental Contamination with Beryllium Phosphor. Nichol, A. D. and Dominguez, R.: *J. Am. M. Ass.*, **140:** 855, 1949.

The authors refer to the relatively high incidence of chronic pulmonary granulomatosis following exposure to high beryllium content phosphor, despite the failure to produce such changes in experimental animals by exposure to beryllium compounds. From examination of tissues and urines from patients so exposed, and clinical observation, it is believed that zinc beryllium silicate is the cause of such disease. They infer from their experience in two reported cases of cutaneous granulomas following accidental laceration of the skin with broken fluorescent light bulbs, in which the phosphor was of low beryllium content, that the beryllium content is of minor importance in the cause of the serious industrial diseases following exposure to beryllium phosphors. The patients had been exposed to beryllium-contaminated air while working in the fluorescent bulb industry for 4½ and 6 years respectively. Both developed the characteristic syndrome which had been observed in other cases associated with roentgenologic and histologic appearance in chronic beryllium granuloma of the lung. Both accidentally lacerated the skin with broken fluorescent light bulbs. The wounds in each case were sutured and healed promptly, but the scars subsequently became hypertrophic, painful and tender. The affected tissue was widely excised and portions subjected to histologic study. Spectrographic analysis of the tissue in each case showed the presence of beryllium. A "control" scar unrelated to injury from broken glass bulbs examined in one case showed no beryllium, neither did it show the characteristic granulomatous structures found in the scars of contaminated tissue, which the authors denominated as "sarcoids", and of which a number of photomicrographs illustrate the article. The surgical removal of the beryllium deposits traumatically produced in the skin had no demonstrable effect on the pulmonary lesions. The authors consider that the pathological behaviour of cutaneous and subcutaneous tissues which were the site of beryllium deposits for 8½ years supports the clinical evidence that beryllium is at least a major factor in the causation of a sarcoid-like disease in other tissues, although there is no suggestion that pulmonary disease resulted in the cases reported from cutaneous deposits. It is claimed that the cure of local lesions demands complete removal of all contaminated tissue, and preventive measures should include wide excision of the original wound before initial closure. D. E. H. CLEVELAND

Dermatitis Venenata from Organo-Mercurial Compounds. Gaul, L. E. and Underwood, G. B.: *J. Am. M. Ass.*, **140:** 860, 1949.

The use of such compounds as merthiolate and metaphen for wound disinfection has become widely popularized among members of the profession and the laity. The authors present clinical and experimental evidence that while normal, unbroken skin can withstand repeated applications of mercurial antiseptics before it develops sensitization dermatitis, any breaking down of the normal protective barriers furnishes the first prerequisite for these chemicals to induce acquired sensitization. Patch-tests, unless the skin has been sensitized by prolonged exposure or interruption of the protective barriers will thus be negative. The sensitization dermatitis when the chemical has been applied for wound disinfection is commonly mistaken for secondary infection and is treated with further applications, to the discomfiture of patient and doctor. Merthiolate, in the authors' experience, had the highest exposure ratio and thus produced the greatest incidence of dermatitis. The specificity of these sensitizations is remarkable. For instance a patient sensitized by merthiolate gave a negative response to patch-tests with mercresin, ammoniated mercury, metaphen and mercuric chloride. Numerous common dermatoses of non-infectious or non-bacterial origin are routinely treated by the laity or their physicians with organic mercurials, resulting in large numbers of cases of over-treatment dermatitis. When a positive patch-test to mercurials appears it indicates that a generalized sensitization has occurred. In view of the high specificity of the various organic mercurials group reactions are better explained as past treatment exposures rather than as examples of multiple sensitivity. There is a tendency in our therapeutic measures to invoke the ready powers of mercurials, including inorganic compounds and to produce generalized sensitization as well as epidermal and dermal. In the presence of cutaneous sensitization to ammoniated mercury an explosive, generalized, urticarial, eczematized dermatitis has followed the internal administration of calomel. Sudden death has followed the injection of mercurial diuretics, and the authors suggest that before they are given, a patch-test with mercury should be used to exclude the possibility of the existence of epidermal sensitization. D. E. H. CLEVELAND

Further Studies in the Use of Furacin in Dermatology. Downing, J. G. and Brecker, F. W.: *New England J. Med.*, **239:** 862, 1948.

This report, from the Boston City Hospital Dermatological Department is made on a series of 278 cases of various classes of dermatoses. Furacin (5-nitre 2-furaldehyde semicarbazone) was used in the form of the soluble dressing as usually sold, and solution. The soluble dressing base was used in two forms, one with propylene glycol and the other with polyethylene glycol, and the solution used was polyethylene glycol.

Former experience that the preparation is most effective in pyogenic infections — impetigo contagiosa, ecthyma, and hypostatic and decubitus ulcers—and is of some value in infectious eczematoid dermatitis was corroborated. Preliminary patch-tests with dressing and solution made up with polyethylene glycol on 25 volunteers elicited only one positive reaction, but in clinical experience it was found that reactions occurred in several cases with the polyethylene glycol and the reactions were again elicited after recovery, while minimal reactions or no reactions occurred with the original soluble dressing. The authors consider that furacin is an effective bactericidal agent, that substitution of polyethylene glycol causes little or no sensitization of normal skin, but that in cases under treatment sensitization developed in over 6% of cases. They consider that the sensitization is due to a synergistic action of the furacin powder plus ethylene glycol on abnormal skin, that this develops only after some time of use or repeated use, and that preliminary patch-tests are of no value. They therefore advise careful selection of cases and the supervision of patients using such compounds. D. E. H. CLEVELAND

Prurigo of Hebra. Zavaleta, A. T. and Mom, A. M.: *Arch. Dermat. & Syph.*, **57:** 998, 1948.

This disease, hitherto most prevalent in Austria, rarely encountered and then usually in a mild form, amongst the native North American population, is described by the writers, in the Department of Dermatology and Syphilology of the University of Buenos Aires Faculty of Medicine, as observed in two patients, one a native Argentinian and the other a Viennese youth. With the large population shifts since the World War, it may be anticipated that more cases will be encountered by Canadian and American dermatologists. The disease generally begins during the second year of life and per-

sists for indefinitely long periods. The eruption consists of successive crops of persistent itchy papules, which eventually disappear without a trace and in recurrences the eruption becomes more profuse. Scars may result from severe scratching, and lichenification, especially at knees and elbows, commonly occurs. The distribution—sparing largely or completely the head, flexures palms and soles, and the excessive involvement of the legs in contrast to the arms and limbs in contrast to the trunk—is pathognomonic. The disease preponderates in the male sex and in Jews. Environmental factors such as the dietary deficiency and lack of personal hygiene which accompany poverty are important. In the opinion of the authors the disease is essentially an atopic dermatitis, and diphenhydramine (benadryl) in daily dosage of 150 to 200 mgm. is of distinct value. Elimination of environmental factors by institutional care, dietary supervision with large amounts of A and D vitamins, ferrous salts and calcium with local care which included daily bathing are also necessary. The measure of success attending these procedures removes the disease from the class of incurable.

D. E. H. CLEVELAND

Pathology

Cholecystitis. Weismann, R. E. and McDonald, J. R.: *Arch. Pathol.*, **45:** 639, 1948.

The authors reviewed the prevalent theories regarding the etiology and pathogenesis of cholecystitis as well as its histopathological features. They cited the frequent absence of significant bacteriological findings in acute cholecystitis and compared its microscopic appearance with that of other lesions, *e.g.*, fat necrosis, lipoid granulomas, comedomastitis, etc., whose pathogenesis is said to involve irritants of a lipoid nature.

Twenty-three gall bladders which showed evidence of advanced inflammation and intramural deposits of lipoid material were examined microscopically. Five of these, as well as seven additional gall bladders, were also subjected to chemical analysis. Marked fibrosis was found involving particularly the subserosal and perimuscular portions of the wall. Abscesses were encountered in about one-half the specimens. They showed a cellular exudate characteristic of chronic inflammation and were usually located in the subserosa. Fat stains demonstrated large amounts of intracellular fat in these lesions. Four cases showed granulomatous lesions characterized by large numbers of giant cells and "foam cells". Seven specimens showed the presence of bile pigment in the subserosa. Eight cases showed the presence of Rokitansky-Aschoff sinuses and in one case one of these sinuses was intimately associated with a subserosal abscess. Four of the five cases which were analysed chemically showed a mean total cholesterol content of more than eight times that of those gall bladders which showed only minimal inflammation. The cholesterol content of one of the specimens was twice that of the controls. The fatty acids were also elevated, but the lecithin content was not significantly altered.

The authors concluded that lipoid irritants, particularly cholesterol and cholesterol esters, may be of considerable etiological significance in many cases of cholecystitis. They regarded the Rokitansky-Aschoff sinuses of importance in the development of these lesions as well as in many cases of bile peritonitis in which no perforation of the gall bladder could be demonstrated.

F. A. JAFFÉ

Anæsthesia

Nupercaine Spinal Anæsthesia for Upper Abdominal Surgery of Long Duration. Stechishin, O.: *Anæsthesiology*, **10:** 494, 1949.

The author describes a new technique for spinal anæsthesia employing a combination of isobaric nupercaine (1:200) and hypobaric nupercaine (1:1,500) which in a series of 37 cases has afforded anæsthesia of long duration for surgery of the upper abdomen, most of the series being for gastrectomy. The technique is another modification of the original Etherington Wilson employing the setting up position for the injection of the two drugs. In general 2 c.c. of the isobaric nupercaine solution (1:200) are injected first through the third lumbar interspace with the patient sitting bolt upright and the head fully flexed, followed almost immediately by the subsequent injection of 15 c.c. of hypobaric nupercaine (1:1,500). The time taken for the injection of the light nupercaine is forty-five seconds from the commencement of the injection until the patient is promptly placed in about 20 degrees Trendelenburg which limits the upward diffusion of the hypobaric solution. Anæsthesia promptly develops to about the level of the nipple line with little subsequent rise of level.

The degree of relaxation obtained by the technique is quite marked and the duration much more than usually expected with single injection methods as contrasted with continuous spinal. The largest spinal anæsthesia in the series was four hours and forty-five minutes, the duration of the operation. The bowels were markedly contracted as is desirable for this type of surgery.

The author feels that the combined volume of the two solutions: 2 c.c. + 15 c.c. or 17 c.c. is safer in practice than the use of 20 c.c. of the light nupercaine alone as is often done. The concentrated solution of nupercaine (1:200) reinforces the action of the smaller quantity of the hypobaric nupercaine (1:1,500) and gives a much longer action than larger quantities of the more dilute solution used alone.

The technique appears to be a useful and safe procedure for gastric resections and difficult surgical procedures on the biliary tract even in poorer risk patients and older age groups. If spinal anæsthesia is selected for major abdominal surgery, particularly the upper abdomen, the combined nupercaine technique affords excellent operating conditions with a minimum of postoperative complications. It may be used in place of continuous spinal anæsthesia.

F. ARTHUR H. WILKINSON

Psychological Medicine

The Incidence of Allergy in Psychotic Reactions. McAllister, R. M. and Hecker, A. O.: *Am. J. Psychiat.*, **105:** 843, 1949.

This paper has a bearing on the possible relationship between allergy and neurotic difficulties, since a psychotic reaction is considered to preclude the presence of neurotic stress. The authors studied, by history and objective examination, the incidence of allergic manifestations in 1,875 neuropsychiatric patients, mostly psychotic, and 757 control individuals among hospital personnel. By history, the controls presented 20% with allergic symptoms compared with 5.7% among the patients, but the histories from the patients were not comparable with those from the non-psychotic controls. By comparable physical examination the controls manifested 13% of allergic phenomena compared with 2.9% among the patients. Epileptics, however, comprised one group of patients with 13% showing allergic signs. These findings would appear to represent an interesting psychobiological phenomenon, although need for repetition of the study is suggested by some carelessness in the analysis of the data, *e.g.*, lumping psychopathic personality with organic psychoses, "to complete the statistical data".

W. DONALD ROSS

Rôle of Emotion in Glaucoma. Sykes, C. S.: *Dis. Nerv. Sys.*, **10:** 104, 1949.

This is a report on the physiological effects of emotional tension on the eye through its autonomic innervation, and describes four cases of glaucoma with evidence of emotional factors as precipitants for individual attacks.

The first was a 32-year old woman, whose prodromal symptoms of blurred vision with halos around the lights

occurred following her husband's death in a train wreck. Her first acute attack of glaucoma occurred following mydriasis for refraction, and it necessitated iridectomy on the right eye. Subsequent mild attacks in the eye could be correlated with emotional upset, but they could be cut short by the prompt use of pilocarpine instillation and reporting to her doctor to discuss the emotional situation. Twenty years after the operation on the right eye, tension was 20 in each eye, and she had weathered the stress of a son being in the Pacific during the War. The second patient had an operation on one eye for an attack precipitated by financial reverses of her husband, and she was warned about what to do in the event of recurrence of symptoms. She went for ten years without symptoms, but when her husband announced his intention to divorce her, her trouble recurred. She did not carry out the ophthalmologist's instructions and she had to have an operation on the second eye. The third case was a 39-year old man with attacks directly related to difficult working conditions or a threat of reduction in salary. One severe attack followed an alarmist attitude by another ophthalmologist to his condition, and it was relieved by reassurance from the author. The fourth was a woman with normally functioning eyes at age 67 and 72, with a sharp rise in ocular tension and rapid deterioration of vision following her husband's death when she was 73. The author also mentions attacks brought on by fear of surgery, and he emphasizes the rôle that the ophthalmologist can play in improving the mental outlook of these people, pointing out that psychiatric consultation may be advisable, but that it is even more important for the ophthalmologist to be aware of how these people react to stress. This paper is important because there have not been many publications on the psychological aspects of glaucoma, and it demonstrates the practical handling of these by a non-psychiatrist. W. DONALD ROSS

Industrial Medicine

Personal Factors in Industrial Accidents: A Study of Accidental Proneness in an Industrial Group. Wong, W. A. and Hobbs, G. E.: *Indust. Med.*, **18:** 291, 1949.

It has been repeatedly demonstrated that chance or risk of a specific occupation are not the only factors in acident causation. Certain workers possess certain personal characteristics that make them more prone to have accidents than others. The purpose of this study was to attempt to assess the practical use of the extensive information that has accumulated on the subject of accident proneness in industrial groups. The accident records of a large modern industry were reviewed and a department chosen that offered the best facilities for statistical study. The accident rate here was much higher than in other divisions; the accidents were minor; the relative basic risk per worker was relatively constant and the accident prevention program had been emphasized.

Over a period of four weeks there were 1,642 accidents among 290 men. Almost one-half of the workers had less than five injuries during this period and the greatest number of men had only one accident. Yet during this same interval five, or 1.7% of the men had more than 20 injuries and account for 6.8% of the total calls at the medical department. The mean accident rate was 5.7 whereas the rate would have been 2.6 if chance alone was responsible. The findings confirmed previous beliefs that accident proneness is a lifelong characteristic and it appears to invade all aspects of life. Other reports have shown that the group who have the most frequent minor accidents also have an undue proportion of major accidents.

The factors responsible for these tendencies were obtained by studying the personality characteristics of the 17 members of the high accident group and comparing them with a similar number of workers having a low accident record. The groups differed markedly in their social adjustment. The high accident worker came most frequently from a broken home, had had conflict with authority in both childhood and adulthood, had a poor work history, and a record of marital discord and contact with social agencies. The aggressiveness that led to difficulties in their personal life is the same factor that leads to a high accident record at work.

Accident proneness is not a subject of limited academic interest but is important to the industrial physician. A personal interview and the taking of a more detailed personal history will reveal the more extreme examples of this group and should be introduced whenever a worker is being hired for a job that is potentially dangerous to himself or others. Individual accident records should be so maintained that a high accident experience becomes immediately apparent and is followed by a determination of the worker's pattern of reaction. A worker who is markedly accident prone should be transferred to a less dangerous occupation. Lifelong emotional reactions are rarely influenced by reason or education.

J. F. SIMPSON

The Epileptic in Industry. *Indust. Med.*, **18:** 45, 1949.

Modern medical knowledge and employment practices give a new approach to the problem of the epileptic in industry. In this editorial favourable opinion is expressed as to their employment, provided they are placed in a suitable working environment. Under such conditions most of the grand mal and petit mal epileptics can and should be employed with the same expectation as to satisfactory production, safety and absentee records as has been demonstrated by persons with certain defects.

Modern treatment has introduced a new era in the handling and prognosis of most epileptics. In so far as the grand mal and petit mal types are concerned, the elimination of seizures can be almost completely assured by the regular and correct use of certain new drugs. The outlook for those persons suffering from the psychomotor type of epilepsy is not the same. Frequently they are not employable. Those cases, however, with unfavourable implications as to employment, comprise less than 25% of all epileptics. When properly placed, epileptics should be expected to meet production standards and have no appreciable allowances made for them. The editorial draws attention to the fact that it is desirable to place them in non-hazardous jobs so that they endanger neither themselves nor their fellow employees, and to guard against the possibility of an untoward event occurring. Education concerning all problems associated with epilepsy is important for employers, physicians, employees and the general public. Through correct treatment, co-operation by the employee concerning his treatment, and the principles of selective placement, the stigma attached to epilepsy can be eradicated. Establishment of a case-finding campaign to find unknown epileptics so that they may receive correct treatment, would be another important measure.

MARGARET H. WILTON

Vertigo. Hagens, E. W.: *Indust. Med.*, **17:** 488, 1948.

The author distinguishes between diagnosis and true vertigo. Dizziness is a sensation of unsteadiness with a feeling of movement within the head; true vertigo—a disturbance of equilibrium—is a sensation as if the external world were revolving around the patient, or as if he himself were revolving in space. With patients suffering from either condition it is important to obtain as complete a history as possible. All causes must be considered, as otherwise an incorrect diagnosis may be made, with resultant improper evaluation and treatment. The following information is essential: presence or absence of deafness, of nausea and vomiting, and of nystagmus; any history of previous illness or injury, or exposure to chemicals or of ingestion of drugs; time and manner of onset of the vertigo, and its duration or recurrence.

Frequently cases of true vertigo can be solved by following a simple classification that considers the site

and origin of the disturbance: (1) local conditions involving the ear; (2) any irritation involving the eighth nerve; (3) involvement of the intracranial pathways; (4) ocular conditions such as muscle imbalance; (5) changes in quality or quantity of blood supply to vestibular tracts; (6) toxic action on the 8th nerve or the central pathways from a number of causes. This includes chemicals from paints and varnishes.

Certain laboratory tests which are of value as an aid to diagnosis, are outlined. In the author's opinion the prognosis of any cases of vertigo depends upon the success of finding the proper etiological factor, and whether such a cause is amendable to treatment. He discusses this aspect, and also that of treatment.

Reference is made also to Menière's symptom complex —one outstanding cause of vertigo.

MARGARET H. WILTON

OBITUARIES

Dr. J. O. Albert Beaupré of Buckingham, Que., died July 20, at St. Michael's Hospital following a short illness. He was a graduate of Laval University in Montreal and practised his profession of medicine at Malone, N.Y., for 20 years, and in Point St. Charles for 45 years, retiring two years ago when he came to Buckingham to reside. He was born at Ste. Elizabeth, Que., on May 12, 1862. Surviving are two sisters.

Dr. George Alexander Berwick died on July 23 in his 86th year at the Montreal Convalescent Hospital. He was born in Farnham, Que., March 5, 1864. He entered McGill University in 1884 from which he graduated with the degrees, M.D., C.M., in 1892. He served his internship at the Montreal General Hospital. Always closely affiliated with church work, Dr. Berwick was keenly interested in the campaign in 1925 for the union of the Presbyterian, Methodist and Congregational churches. As a member of the Presbytery of Montreal for over 50 years, he was one of those responsible for the formation of the United Church of Canada. He was an active member of Waverly Lodge 82, A.F. & A.M., and the St. Lawrence Curling Club for many years. Survivors are a son, a brother and two grandchildren.

Dr. F. E. Chabot, who practised medicine for 28 years in Quebec City, died July 25 after several months of illness. He was 56. He was a former president and founder of the St. Jean Baptiste Medical Society. He is survived by his wife, three sons, two daughters, one brother and four sisters.

Dr. Harvey Clare, aged 77, died at his home in Guelph, Ont., on August 5. Born at Tweed, he was educated at Sterling High School, Albert College and Trinity University where he graduated in medicine as gold medallist in 1896. Specializing in psychiatry, he entered the provincial government medical service shortly after his graduation.

Dr. Clare served as superintendent of Homewood Sanitarium at Guelph for 17 years and on his retirement in 1942 continued as consultant to the Department of Justice in Ottawa. He is survived by his widow and two sons.

Dr. Arthur R. Deeley, former resident of London, died suddenly on August 23, at his home in Regina. Surviving are his widow, two brothers and two sisters.

Dr. Jos. Desjardins est décédé le 20 juillet à Québec à l'âge de 57 ans, après une longue maladie.

Il avait fait ses études classiques au collège de Ste-Anne-de-la-Pocatière. Il obtint son brevet de docteur en médecine à l'Université Laval de Québec en 1918. S'étant enrolé au R.C.A.M.C., il fut attaché au C.O.T.C. Laval, puis fut chargé des soins médicaux sur les trains de blessés ou des soldats rapatriés. Il fut pendant 21 ans, médecin résident de St-Marc-des-Carrières, où il prit une part très active aux organisations religieuses civiles, politiques et patriotiques. A la déclaration de la dernière Grande-Guerre, s'étant enrôlé de nouveau, il fut nommé officier médical du Régiment de la Chaudière, avec lequel il se rendit jusqu'au camp de Sussex, N.-B. Là la maladie qui devait l'emporter, vint le terrasser, au printemps de 1941. Il laisse outre son épouse, deux fils, deux filles, trois frères, et deux sœurs.

Dr. W. Ewart Ferguson, aged 61, for the past 25 years chief medical referee for the Excelsior Life Insurance Co., died from a stroke at his home in Toronto on August 11. Born in Toronto, he was the son of the late Dr. John Ferguson, prominent physician and founder of the Toronto Western Hospital. He was also medical director for the Norwich Union Life Insurance Co., Dominion of Canada Assurance Co., and the Sun Insurance Co., Wellington St. Dr. Ferguson graduated in medicine from the University of Toronto. For a time he was chief pathologist and chief bacteriologist at the Toronto Western Hospital. He was a member of the Ontario Medical Association and Rosedale Golf Club. He leaves his widow, a brother and a sister.

Dr. Robert Burrows Harris died in Toronto on August 14. Confined to the Toronto General Hospital, where he underwent an operation on July 12, he was making steady progress when stricken with coronary thrombosis. He was in his 70th year. A pioneer medical man with the International Nickel Company hospital at Copper Cliff, serving throughout the Sudbury district for the past 35 years, Dr. Harris retired from active practice in February, 1946.

A native of Charlottetown, P.E.I., he graduated from the University of Toronto in the early 1900's, and first hung out his shingle at Campbellford, Northumberland County where he remained a year, and then left to become camp doctor in a number of lumber camps in the area north of Blind River. He later moved to the Magnetawan. He moved to Copper Cliff in February, 1911. Dr. Harris worker in the various Inco towns of the entire Sudbury area. He served with the Royal Canadian Army Medical Corps in England, France, Belgium and Germany in the First World War, earning for himself a distinguished war record, administering to the wounded on the battlefronts of Europe. He returned to Canada in 1919 to resume his post with Inco. Dr. Harris was a member of the Masonic Lodge, and some 33 years ago, organized the Elks Lodge in Copper Cliff. He was an ardent outdoorsman and spent many happy days at his summer camp at Birch Island. He was a familiar figure on the island, during summer months, casting a rod, dressed in an old pair of slacks, and a battered fishing cap. A bachelor, he is survived by four sisters.

Dr. Eldridge Tyler Kellam, aged 78, died at his home in Niagara Falls, Ont., on September 3, 1949, after a long illness. He was born in Lucknow, Ont., on July 11, 1871. He attended the High School in Seaforth and graduated from the University of Toronto, Faculty of Medicine in June, 1895. Later that year he settled in Niagara Falls where he had been in general practice since. On June 23, 1945, he received the M.D. degree from the University of Toronto in recognition of 50 years of practice. He took an active interest in medical organizations and became president of the Niagara Falls Medical Association and the Niagara District Medical Association. When the Ontario Medical Association met at Niagara Falls in 1910, 1920 and 1930, he acted as chairman of the committee on arrangements on each occasion. In 1915 he was elected to represent District No. 4 in the College of Physicians and Surgeons of Ontario where he served for twenty years. He was president of the College in 1923-24. Dr. Kellam was prominent in the educational life of the city having been a member of the Board of Education for 48 years. He took an active part in the erection of the Niagara Falls

General Hospital in 1904 and was a member of the Greater Niagara Hospital Trust until his death. He was a past President of the Niagara Falls Rotary Club and a former superintendent of the Morrison Street United Church Sunday School. He is survived by one daughter and one granddaughter.

Lieut.-Col. Henry Ernest Kendall, M.D., former Lieutenant-Governor of Nova Scotia, died at his home in Windsor, following a lengthy illness, September 3, 1949. Dr. Kendall served as Lieutenant-Governor of Nova Scotia from 1942 to 1947, retiring in the latter year because of ill health. Since that time he had been living on his farm at Windsor. He was born at Sydney, April, 1864. He was educated at Sydney Academy, received his arts degree from Mount Allison University, and studied Medicine at McGill University, completing his course at Bellevue Hospital, New York. From 1888, until the outbreak of World War One he practised in Sydney, with the exception of a short time in practice in St. John's, Newfoundland. For a time he held the post of Provincial Registrar in Halifax. When St. Francis Xavier Hospital Unit was organized, Dr. Kendall joined the unit as second in command with the rank of major and went overseas in 1916, serving at Bramshot, Etaples and Shorncliffe. After the death of Lieutenant-Colonel R. C. McLeod, the commander, Major Kendall was appointed lieutenant-colonel and assumed command 1917. In 1918 Dr. Kendall returned to Canada and was placed in charge of surgery at Camp Hill Hospital, a post he held until he returned to civilian practice a year later. In the early 1900's he was one of the pioneers of the use of x-ray for the treatment of cancer. Resulting x-ray burns on his hands in later years necessitated amputation of several of the fingers of both hands. Dr. Kendall was an ardent fisherman and yachtsman and travelled extensively in America and Europe.

Dr. William S. Lehto died suddenly on August 24 at his home in Toronto. He had suffered from a heart condition for several years. He was 40. Dr. Lehto was born in Finland, came to Canada with his parents when a year old, and the family settled in St. Catharines. He worked his way through Queen's University medical school, graduating in 1933. He was a keen baseball and hockey fan, and since the war had been active in various groups organized to assist new immigrants in Canada. He published several magazine articles on medical subjects. He is survived by his widow, and his 3-year-old daughter.

Dr. John M. McDonald who had been practising medicine in several Saskatchewan towns during the past five years, died in Limerick on August 14. At the time of his death, he was practising in Glenn Kerr, north of Morse. Dr. McDonald was formerly professor of anatomy at Toronto.

Dr. P. A. McDonald died at his home in Penetanguishene on August 13. Born in Alexandria, in 1863, he graduated from McGill University in 1889, and practised medicine for several years in Pueblo, Col., before coming to Penetanguishene in 1897. For many years he was chairman of Penetanguishene High School Board, and Medical Health Board. He was predeceased by his wife 12 years ago, and is survived by three sons, two daughters, and two sisters.

Dr. J. E. Racicot of Montreal, died of a heart attack at Old Orchard Beach, Me., on July 23 while on a vacation with his wife. He was 70. Born in Montreal, he studied at Mont Saint-Louis and College Sainte-Marie. He obtained his degree of doctor of medicine from Laval University in 1903. He was an anæsthetist at Notre Dame Hospital for 30 years, and was known internationally having served as a councillor of the International Anæsthetist Society for two years. He also served on the Medical Board of the Canadian Army from 1940 to 1945. Dr. Racicot was a past director of the Société des Artisans Canadiens-Français, as well as past president of the Canadian Society of Anæsthetists and an honorary member of the Fusiliers Mont-Royal. Surviving are his widow, six daughters, two sons, two sisters, two brothers and a half-brother.

Dr. Charles E. Rowland died in Chatham General Hospital on July 19, aged 69. Resident of Wallaceburg for over 40 years, he was an honour graduate of the University of Toronto, taught school for several years and then took his studies at the School of Medicine. He is survived by his second wife, a son, two daughters, a brother, and two sisters.

Dr. John Wesley Russell, medical practitioner for 40 years, died on August 27 at his home in Toronto. He was born at Kirkwood, Ont. Graduating from high school at the age of 15, he farmed for a year, then entered Medical College at the University of Western Ontario, London. A Toronto alderman for one year, Dr. Russell also represented Ward six as a school trustee for several years. He was active in football at Western and later interested in baseball, hockey and football. He was former club doctor of the old Toronto Ball Club. He was a member of the United Church and Alpha Lodge, A.F. & A.M. Surviving are his widow, one son, two daughters, three sisters and one brother.

Dr. John Frederick Sadleir died in his 70th year at his home in Sarnia, Ont., on August 5. He had been in ill health for some time. Born in St. Paul's, Ont., he received his early education in Lucan and Strathroy and on completion of his studies there entered Wycliffe College, Toronto. He later graduated in medicine from the University of Manitoba in 1913. Dr. Sadleir practised medicine in Winnipeg until 1915 when he proceeded overseas with the Royal Army Medical Corps and saw active service in France. He was an active member of St. John's Anglican Church, from which he was a delegate to the Synod of the Diocese of Huron. Surviving are his widow, a daughter, two sons, six grandchildren, a sister and a brother.

Dr. David Emerson Scott, aged 59, well-known Wiarton and Beardmore physician, died at the home of his brother, in Ferndale, Ont., on August 9. Born in Eastnor Township he received his early education in Wiarton and Owen Sound. Graduating from London Medical College, he joined the Royal Canadian Medical Corps in the First World War, serving in the Near East and French theatres of war. Following the First World War he served with the R.C.M.P. in Aklavik and then spent five years with an oil company in Iran. In the Second World War he served as a major on convoy duty. Surviving are four brothers and one sister.

Dr. P. F. Smith died in Camrose, Alta., on July 8. Born in Badeque, Prince Edward Island, on March 25, 1873, he studied medicine in the Johns Hopkins Institute of Surgeons and Physicians at Baltimore, Maryland, after he had attained his B.Sc. degree. He always held it a high privilege to have taken lectures for four years under Sir William Osler. He came to Alberta in June, 1910. In 1912 he was appointed medical examiner for the Provincial Normal School in Camrose and retained that office till the school closed. In 1923 he was appointed Medical Health Officer for the Town of Camrose, retaining that office till 1948, when it was taken over by his son, Dr. Mac. Smith. He also held the appointment of surgeon for the local district of the C.P.R. for several years, and held the office of Coroner from 1915 till 1947. He was one of the very few physicians in Alberta to retain membership in the American Medical Association. He was a member of the Camrose Masonic Lodge, having filled the chair of Master during the year 1926. He also was a Shriner, of

Al Azhar Temple, Calgary. He was a charter member of the Camrose Rotary Club and was honoured by a life membership in 1946. He was an active member of the Camrose Board of Trade for many years and was signally honoured at the annual meeting in 1948, along with Frank Farley, with an honorary life membership. He was a keen horticulturist and rejoiced in the culture of fine blooms, particularly gladioli, and his garden was always a picture.

Dr. Stanley C. Suffel, aged 52, died of a coronary thrombosis in St. Francis General Hospital, Smiths Falls, Ont., on August 5. Born in Smiths Falls, he attended the local schools and collegiate institute, afterward entering the University of Toronto from which he graduated in medicine in 1924. He was a member of St. Francis Lodge, ROM Canadian Order of Foresters, and Trinity United Church. Besides his widow he is survived by three sons, two daughters, two sisters, and a brother.

Dr. Thomas B. Underhill died on July 18 in hospital in Moose Jaw, Sask., at the age of 69 years. He was born in Brantford, Ont., and came to Moose Jaw 45 years ago, taking employment with the railway mail service, and also attending McGill University, where he studied medicine, graduating from there in 1910. He was a keen tennis player and his athletic activities also included badminton and golf. Dr. Underhill was a member of the masonic order, being a past master of the St. George Lodge No. 136, A.F. & A.M.

Dr. Elizabeth N. Warner, well-known Montreal pædiatrician died August 9 at the Ross Memorial Pavilion of the Royal Victoria Hospital following a brief illness. Born in Brookline, Mass., Dr. Warner was a graduate of Vassar College and in 1932 obtained her degree of medicine from McGill University. She was also the holder of the diploma of the Royal College of Physicians and Surgeons. After experience on the staff of hospitals in Toronto, New York, London and Copenhagen Dr. Warner joined the staff of the Montreal Children's Memorial Hospital. She became a British subject in 1929. She is survived by her mother, three brothers and by two adopted daughters.

Dr. Samuel T. White died of a cerebral hæmorrhage at his home in Orangeville, Ont. on August 29. An ardent lacrosse player and golfer in earlier years, Dr. White more recently was a keen curler. Last season he was president of the Ontario Curling Association. He graduated in medicine from the University of Toronto in 1907 and took postgraduate studies in New York and Edinburgh. He practised in Shelburne for 20 years before coming to Orangeville in 1927. A member of the Shrine and Westminster United Church and a Fellow of the American College of Surgeons, he is survived by his widow, three daughters, a sister and a brother.

NEWS ITEMS

Alberta

Dr. Morley Tuttle of Lethbridge is taking postgraduate work in internal medicine in Eastern Canada and the United States, Dr. Tuttle is associated with the Campbell Clinic in the Southern City.

Dr. Allan J. Lobsinger of Edmonton has returned to his practice following a year in postgraduate surgery at the University of Edinburgh, while away Dr. and Mrs. Lobsinger visited the Continent.

The Department of health of the Province is setting up facilities for the treatment of certain types of arthritis in young individuals, this treatment and investigation will be free to the individual. Dr. Kenneth Thompson was named Director. The first clinics are to be held in the Col. Belcher hospital in Calgary.

Dr. Jean Holowach, specialist in pædiatrics, gave up her practice in Edmonton and upon her marriage is now living in St. Louis, Mo. We wish her continued success in her two well chosen fields. Dr. Holowach's husband is also a pædiatrician of St. Louis.

Dr. Brock Armstrong has taken Dr. Holowach's office in Edmonton and is specializing in pædiatrics.

Dr. R. W. Robinson, a graduate of Toronto is now associated with Dr. J. F. Brander of Edmonton. During the war he was with the R.C.A.M.C. following which time he was in practice in Baie Verte, Newfoundland, for two years. Dr. Robinson did his postgraduate work at St. Michael's Hospital in Toronto before coming to Edmonton with his wife and family.

Dr. R. G. Douglas of Edmonton is spending his holidays in Ontario his native province and will return to his practice in October.

Dr. C. M. Learmonth of Edmonton announces the opening of his private practice in anæsthesiology. Dr. Learmonth received his certificate in this specialty from the Royal College of Physicians and Surgeons of Canada.

W. CARLETON WHITESIDE

British Columbia

The latest press reports about the progress of the British Columbia Hospital Insurance Act show that a deficit of some $3,000,000 is expected for 1949. Just how this will be met is not quite certain, though a recent speech by the Premier, the Hon. Byron Johnson, foreshadows a rise in dues, of some 40% for single people, and considerably less for married people or families. This suggestion has met with considerable opposition in some of the newspapers which have commented editorially on the matter.

The 3% sales tax, which was imposed with a view to meeting the costs of social services in the Province, on the other hand, is expected to provide a sum of some twenty millions, which is a good deal in excess of the amount expected. Perhaps one hand may be able to wash the other in this regard and some of the deficit in the Hospital tax met in this way.

The polio epidemic continues to provide its daily quota of cases, though for a short time the number seemed to be abating. No more deaths have been reported, however, and the disease is of a relatively mild type.

The new Medical Faculty of the University of British Columbia is assuming shape rapidly. Dean Weaver has been very busy organizing the work for the pre-clinical years, and has recently returned from a trip to eastern centres, which he visited to secure personnel for teaching. At the outset, the new Public Health and Preventive Medicine buildings at the University will be used for classes, until the new medical buildings proper, soon to be constructed, are ready.

The Royal Columbian Hospital of New Westminster is undertaking a program of building in the immediate future. This new extension will double the present bed capacity of the hospital.

The town of Enderby is also in the business of hospital construction. It has received the go-ahead signal from Dr. J. M. Hershey, Commissioner under the Act, and a hospital of twenty beds will shortly be built.

The medical staff of the Vancouver General Hospital has, for the past three or four years, made a yearly practice of inviting some well-known internist as guest chief of medicine for the hospital, his visit covering a week. This has always been a very popular and profitable period, and all medical men are invited. Lectures and clinics are given, and an intensive program is arranged. The medical staff has decided to do this twice in the following year, at intervals of six months. The first of our visitors will be Sir John Parkinson, of London, England, and he will be the visiting chief of medicine during the month of October. He will also address the Vancouver Medical Association at the monthly meeting of that body.

The pædiatric staff of the Vancouver General Hospital has recently published the program of their Second Refresher Course in Pædiatrics, to be held from September 21 to 24, inclusive in Vancouver. The course that was held last year proved to be a very great success, and judging from the printed program, this year's course bids fair to be just as good or better. The meetings will be held in the new auditorium of the British Columbia Tuberculosis Institute, which is admirably fitted for the purpose, as it has all the facilities for the presentation of bed patients, as well as picture screens, loud speakers, and everything to make the lot of the speaker or clinician easy. The North Pacific Pædiatric Society is holding its Annual Meeting in Vancouver at the same time, and has extended a general invitation to all medical men to attend its scientific sessions.

A year ago, the Vancouver General Hospital decided to install a chiropody clinic, in connection with the Outpatient Clinic of the hospital. This clinic is under the direction of the Chief of the Outpatient Department, and receives cases referred to it from the various clinics, and from the hospital at large. During the year, about 1,700 cases have been handled by this clinic. These have come from every department, chiefly the medical and diabetic clinics, as well as the Peripheral Vascular Clinic, but orthopædists, gynæcologists, surgeons, and others, have all found it of value.

The clinic seems to have been thoroughly successful, and to be filling a very definite place in the work of the hospital. The heads of the various departments concerned seem to be unanimous in agreeing that the work done there is of very great value, especially in the case of diabetes and peripheral vascular disease, both from a therapeutic and preventive point of view. The personnel of the clinic, who are all registered chiropodists, cooperate very well with the medical staff, and there is complete harmony at all times. The patients concerned have been very loud in expressing their appreciation.

J. H. MACDERMOT

Manitoba

Dr. D. Roy McCullagh, a graduate of the University of Manitoba, has been appointed director of the biochemical laboratories of the Sterling-Winthrop Research Institute at Albany, New York. Prior to his appointment Dr. McCullagh was director of the biochemical laboratory in the Schering Corporation, Bloomfield, N.J. Born at Douglas, Man., Dr. McCullagh received his M.A., B.Sc., and M.Sc. degrees from the University of Manitoba. He received his Ph.D. degree from the University of Cambridge where he studied as a Nobel prize winner. During the war he set up and operated a scientific laboratory in Cleveland, which specialized in the manufacture of blood plasma and penicillin. At the end of the war Dr. McCullagh headed a scientific commission by the United States Government to appraise scientific laboratories in Germany.

Construction is now well advanced on a new four-storey wing which is being added to the main building of the Provincial Mental Hospital in Brandon. Plans for the new wing were drawn by the Provincial Architect's Department. When completed the wing will accommodate more than 100 beds.

Dr. J. G. Pincock has opened an office at 627 Medical Arts Building, Winnipeg, for the practice of internal medicine.

Dr. Cecil Harris has been appointed provincial medical director for the blood transfusion service of the Canadian Red Cross Society. With his wife and family he will reside in Winnipeg where the new building for the blood transfusion service will be opened shortly. A graduate from the University of Glasgow, he holds degrees B.Sc., M.B., Ch.B., M.D., M.R.C.P.(Edin.). He served with the R.A.M.C. in 1944-45 and on his return to civilian practice was appointed Hall Fellow in Medicine at the University of Glasgow. During the three years of this appointment he did advanced study in internal medicine and hæmatology. He has made a study of transfusion services in the United Kingdom and since coming to Canada served at blood transfusion depots of the Canadian Red Cross Society at Halifax, Montreal and Toronto. Dr. and Mrs. Harris will be welcome in Winnipeg.

ROSS MITCHELL

New Brunswick

Dr. M. I. Polowin, who has been a valued member of the staff of the Lancaster D.V.A. Hospital at Fairville, N.B., for some time has relinquished his post to accept a fellowship in Anatomy at Queen's University.

Dr. Stephen Weyman, has begun a practice in Saint John, confined to pædiatrics. Dr. Weyman has received an appointment as Junior Physician in pædiatrics at the Saint John General Hospital.

Dr. A. E. Macaulay, of Saint John, is recovering from a major surgical operation at the Saint John General Hospital.

The New Brunswick Branch of the Defence Medical Association at their annual meeting at Fredericton, elected the following officers for the year 1949-50. Hon. Pres., Lieut.-Col. D. C. Malcolm, Pres., Major J. A. McLaughlin, Vice-Pres., Major R. F. Ingram, Sec-Treas., Lieut.-Col. J. A. Melanson. Major R. B. Eaton, will represent New Brunswick at the meeting of the Dominion Body at Toronto in October this year.

Dr. Jean F. Webb, formerly of the Nutrition service of the N.B. Dept. of Health, has been appointed an instructor and assistant pædiatrician in the child health division of the Boston Children's Hospital.

A. S. KIRKLAND

Nova Scotia

Dr. P. A. MacDonald of Halifax is seriously ill in the Victoria General Hospital.

Dr. E. A. Brassett, who for the past several years has practised in Antigonish has gone to the United States, where he is presently located in Rhode Island.

Dr. Audley Giffin of Kentville was recently a patient in Camp Hill Hospital where he underwent a serious operation.

Dr. Luther MacKenzie, of New York has been spending the summer at his former home in Bedford.

The medical profession of the Province is looking forward to the annual meeting of the Medical Society of Nova Scotia which will be held at White Point Beach during the week of September 5, and to the

Dalhousie University Refresher Course which will be held in Halifax in October. A feature of the latter meeting will be the first Dr. John Stewart Memorial Lecture, which will be given by the Professor of Surgery, University of Edinburgh, Sir James R. Learmonth.

Dr. William Chisholm of Cape George, Antigonish, and Mount Dora, Florida, is a patient in the Victoria General Hospital, Halifax. Although over 83 years of age he is making an excellent recovery following operative treatment.

All committees are constituted and preliminary work is underway for the annual meeting of the Canadian Medical Association at Halifax in June, 1950. Older members will recall that the 1921 meeting at Halifax, saw the re-birth of the Association.

The course in Public Health and Teaching for graduate, registered nurses, at Dalhousie University sponsored by the Governments of Nova Scotia, New Brunswick, and Prince Edward Island will get underway during September, under the directorship of Electa MacLennan, M.A., formerly Assistant Professor of Nursing at McGill University.

Fifty-eight students have been admitted to first year medicine at Dalhousie University from a large number of applicants. Applications are restricted to bona fide residents of the four Maritime Provinces of Canada.

H. L. SCAMMELL

Ontario

Grants totalling $400,000 have been announced by the Ontario Minister of Health to five Ontario hospitals to enlarge their bed capacity. The Royal Ottawa Sanatorium receives $212,500 supplementing a previous grant of $125,000 to add 135 beds to its present capacity. (Grants to sanatoria are paid on the basis of $2,500 per bed.) Hotel Dieu Hospital, St. Catharines receives $27,000 for a 27 bed addition. The Kingston General Hospital (children's unit) receives $65,000 for 65 beds. Smooth Rock Falls Hospital receives $17,000 and the Red Cross Hospital, Wiarton $66,833 (the province paying one-third of the cost of Red Cross Hospitals). The Wiarton addition is for 22 adults and 11 infant beds.

A grant of $15,700 has been approved by the Federal Government to pay the salaries of four additional public health nurses and two more sanitary inspectors for the Simcoe County Health Unit. Also an additional public health nurse's salary will be paid for the Elgin-St. Thomas Health Unit.

Dr. R. W. Stephens, of London, Ont., has taken over the practice of Dr. J. H. Harper at Brussels, Ont.

Dr. Harry Hotz, is resuming practice in Hamilton, Ont.

Dr. S. S. English has been appointed Coroner for Welland County.

The Halton County Health Unit and the St. Catharines-Lincoln Health Unit are inaugurating preventive dental health services with the aid of funds from the federal health grants. About twenty health units throughout Ontario are obtaining additional technical equipment to increase their services.

An editorial in "*Health*" published by the Health League of Canada points out the slowness with which provincial governments have adopted province-wide laws for the pasteurization of milk. Only two provinces in Canada (Ontario and Saskatchewan) have adequate compulsory legislation the article states.

Starting the week of July 3, from St. John's, Nfld. to Victoria, B.C., 32 independent radio stations have begun broad-casting a series of eight dramatic presentations dealing with venereal disease. This series is being sponsored and distributed in the Dominion by the Health League of Canada. It was produced by Columbia University, New York, in co-operation with the United States Public Health Service. It features such talent as Raymond Massey. In Ontario it will be carried by stations in Belleville, Oshawa, Toronto, Niagara Falls, Hamilton, Brantford, Woodstock, London, Sarnia, Timmins, and Kenora.

New medical, surgical and clinical equipment to improve diagnostic and treatment services in the Ontario Hospitals in Kingston, Whitby, Langstaff, Orillia, Penetanguishene and Fort William will be purchased with money from the Federal Health grants. Federal aid to the six hospitals will total more than $41,000.

NOBLE SHARPE

Quebec

At a recent meeting of the Medical Association of Abitibi the following resolution was passed.

"Il est proposé par le docteur J.-A. Leblanc, secondé par le docteur Edmond Bourgault: (*a*) que chaque province soit chargée de l'administration libre du plan de santé fédéral dans son territoire; (*b*) que le corps médical de la Province de Québec soit représenté dans le comité chargé d'élaborer le plan d'assurance Santé Fédéral; (*c*) que copie de cette résolution soit envoyée au Collège des Médecins et Chirurgiens de la Province de Québec et à la Canadian Medical Association."

Appointment to the two Osler Scholarships have now been made again. These were withheld during the war and for a period thereafter. The recipients this year are Dr. Lester McCallum, and Dr. Hamish McIntosh.

Le docteur Jean Michon membre du personnel de radiologie de l'Hôpital Notre-Dame s'est vu décerné une bourse d'études en rapport avec le British Empire Cancer Campaign. Le docteur Michon s'est joint au personnel de l'hôpital Notre-Dame en janvier 1947 après avoir passé cinq ans dans la marine royale canadienne. Il est actuellement en Angleterre où il doit étudier à Londres, aux hôpitaux Middlesex, Royal Cancer, et Westminster; à l'institut du Radium Holt-Christie, au Edinburgh Royal Infirmary, et à divers autres centres en France, au Danemark et en Suède.

Les doyens des deux facultés de médecine de Montréal, les docteurs Edmond Dubé et Frederick Smith ont été nommé présidents conjoints de l'association nationale de santé.

Le docteur Jean LeSage de Montréal a été élu Fellow de la National Gastro-Enterological Association, Section Américaine, à la séance de mai 1949.

Le docteur J.-Jacques Lussier, assistant en physiologie de l'université de Montréal est le bénificiaire d'une bourse du conseil national de recherches, en physiologie.

Le docteur Charles Guillemette, après avoir terminé sa résidence en chirurgie à l'hôpital Notre-Dame, vient de s'embarquer pour l'Angleterre où il poursuivra ses études.

YVES PRÉVOST

Since the above notes were printed we have to report with the deepest regret, the sudden death of Dr. Frederick Smith, Dean of the Faculty of Medicine of McGill University. Dean Smith was addressing the incoming class of students when he had a sudden seizure, afterwards found to be of cardiac origin and died within a few minutes.

Saskatchewan

Dr. H. D. Dalgleish of Saskatoon has arrived in Great Britain to begin a year of postgraduate work.

Saskatoon's first mental health clinic will open on September 1. The purpose of the clinic is primarily preventive. It is hoped by a broader dissemination of psychiatric knowledge that something can be done to cut down the amount of disabilities from mental disorder. The clinic will provide a consultation and diagnostic service to physicians. It will follow the same policy that was set up after negotiation with the committee on Mental Hygiene for the College of Physicians and Surgeons and for the mental Health Clinic at Regina. All references to the clinic for service will be through physicians. The only exception to this will be those individuals who are wards of Social Welfare. Dr. Z. Selinger, formerly Clinical Director at the Saskatchewan Hospital, Weyburn, will be full time Director of the Clinic.

Dr. M. W. Dobson is at present taking an eight month postgraduate course at Nashville, Tenn.

Dr. M. W. Fujiwara who practiced at Antler has moved to Maryfield; Dr. W. G. Hemenway has moved from Broadview to Porcupine Plains and Dr. J. C. Gough from Porcupine Plains to the Medical Arts Clinic, Regina.

Dr. J. H. Gross, formerly of Fort Qu'Appelle Sanatorium, has accepted a position on the senior staff of the Battey State State Hospital, Rome, Georgia, where he will continue his work in Tuberculosis.

The Annual General Meeting of the College of Physicians and Surgeons of Saskatchewan will take place September 15, 16 and 17 in the Hotel Saskatchewan, Regina. It is to be combined with a meeting of the Annual Refresher Course, under the auspices of the Medical Societies and the Department of Veterans' Affairs in Regina. The scientific program promises to be topical and of selected interest to Saskatchewan physicians. It will also contain some comments on the provision of Health Services in a Health Region. Guests of the College for the occasion will be the President, Dr. J. F. C. Anderson, and the General Secretary, Dr. T. C. Routley, from the Canadian Medical Association; and Dr. L. B. Pett, chief of the Division of Nutrition, Department of National Health and Welfare. A luncheon speaker will be Mr. D. B. Rogers, Editor of the *Regina Leader Post*. The committees of the College have been busy preparing their reports for presentation at the business meeting and the usual informatory discussion is anticipated.

The scheme for supplying medical services in Health Region No. 1 at Swift Current, in the south-west corner of the Province of Saskatchewan has been observed with a great deal of interest by the profession across the country. Interest in this program will be more keen than ever as it is reported that owing to lack of moisture and a poor growing spring, the crop condition in that area is considerably below normal.

Dr. Ernest A. Johnson of Elfros, Sask., who carried on an active medical and surgical practice at that point for over eight years prior to going to Vancouver for postgraduate work last year, has been recently appointed Resident in Ophthalmology at the Vancouver General Hospital. Dr. Johnson was Assistant Resident in the Department of Ophthalmology at the same hospital last year.

G. G. FERGUSON

General

Registration of Technicians. Hospital superintendents, pathologists, and other members of the medical profession are asked to co-operate with the Canadian Society of Laboratory Technologists in an effort to standardize the qualifications and training of laboratory technologists and thus raise the general level of work done in medical laboratories across Canada. Hospital executives are urged to encourage all their technicians who are still unregistered to make application for registration.

Beginning about November 1, Miss Ileen Kemp, President of the Canadian Society of Laboratory Technologists, will make a tour of the western provinces, urging this registration. Tentative plans at the moment are for Miss Kemp to hold meetings in Vancouver, Victoria, Lethbridge, Medicine Hat, Calgary, Edmonton, North Battleford, Prince Albert, Saskatoon, Regina, Yorkton, Brandon, Winnipeg, Port Arthur, Fort William and possibly other centres. Previous to Miss Kemp's arrival in these various centres, announcements will be placed in the local papers.

An invitation is extended to all technicians and other interested persons to attend these meetings so that they may become acquainted with the aims and purposes of the Society. Although no official change will be made in the present requirements for registration with the Canadian Society of Laboratory Technologists each application submitted will be considered individually and registration granted to the applicant upon the individual's merits and recommendations and subject of course, to passing the examinations.

Enquiries should be addressed to the Secretary, Canadian Society of Laboratory Technologists, 294 Barton Street East, Hamilton, Ontario.

The Ambulatory Fracture Association will meet in Toronto, at the Royal York Hotel, October 24 to 27, 1949. A full program has been arranged. Dr. R. I. Harris will be the guest speaker at the Tenth Annual Banquet.

The Physicians' Art Salon. The prize winners in the Physicians' Art Salon sponsored by Frank W. Horner Ltd. of Montreal at the Annual Meeting in Saskatoon this year were as follows:

Fine Art Section. First Prize, Dr. Anna D. Gelber, Toronto; second prize, Dr. John H. Toogood, Montreal; third prize, Dr. H. J. Laudan, Saskatoon.

Monochrome Photography. First prize, Lieut.-Col. C. G. Wood, Ottawa; second prize, Dr. Stuart M. Rose, Lethbridge; third prize, Dr. L. J. Notkin, Montreal.

Colour Photography. First prize, Dr. Griffith Binning, Saskatoon; second prize, Dr. T. M. Jones, Victoria; third prize, Dr. J. F. Burgess, Montreal.

In the Undergraduate Panel the first prize was awarded to John S. Henry of Montreal, and the second prize to D. G. Watson, of Port Credit, Ont.

Messrs. Horner are preparing a full colour brochure featuring the prize winners and their work, to be mailed to all physicians in Canada.

The Salon had a most successful showing this year. It will be held next year in Halifax at the Nova Scotia Hotel. It is proposed to form a new class of competitors composed of previous prize winners who will be put in a higher class and judged separately from other entrants.

The American Urological Association offers an annual award of $1,000.00 (first prize of $500.00, second prize $300.00 and third prize $200.00) for essays on the result of some clinical or laboratory research in Urology. Competition shall be limited to urologists who have been in such specific practice for not more than five years and to residents in urology in recognized hospitals. For full particulars write the Secretary, Dr. Charles H. de T. Shivers, Boardwalk National Arcade Building, Atlantic City, N.J. Essays must be in his hands before February 20, 1950.

A new periodical in a new field will begin publication in February, 1950. It will be called *Angiology, The Journal of Peripheral Vascular Diseases.* Editor-in-Chief will be Dr. Saul S. Samuels, Chief of the Department of Peripheral Arterial Diseases, Stuyvesant Polyclinic, New York City. About 600 pages a year will be published at a subscription price of $8.00. The Williams & Wilkins Company, of Baltimore, will be the publishers.

The American College of Chest Physicians is sponsoring a postgraduate course in diseases of the chest, to be held in New York, November 14 through 18, 1949. Applications for the course will be accepted in the order in which they are received and should be sent to the American College of Chest Physicians, 500 North Dearborn Street, Chicago 10, Illinois.

Defence Medical Association of Canada. The next annual meeting of the Defence Medical Association of Canada will be held in Toronto on October 27 and 28, 1949. All members of the Defence Medical Association are cordially invited to attend.

The Friday sessions will be held in the Royal York Hotel. These will consist of a business session, an address on Civil Defence, discussions on subjects related to Medical Aspects of Atomic Energy, Radioactive Isotopes, Aviation Medicine, Air Transport of Sick and Wounded and Training at Universities and in the Forces generally. At the luncheon and annual dinner to be held on Friday at the Royal York Hotel addresses will be given by leading authorities on some of these same subjects. The Saturday morning session will be held at the Institute of Aviation Medicine when the Association will be the guests of the Royal Canadian Air Force.

The object of the Association is to develop the efficiency of the Canadian Defence Medical Services by the dissemination of knowledge throughout the Dominion on defence medical affairs, thus creating a greater interest among a larger number of medical officers and civilian practitioners. Membership is open to all medical graduates who have served or are now serving in any of the Medical Services of the Navy, Army or Air Force, active, reserve, or supplementary reserve. Further particulars may be obtained by applying to the branch secretaries as listed below:

British Columbia—Major H. Gislason, H.Q., B.C. Area, Vancouver, B.C.; Alberta—Major A. G. McLaren, H.W., Western Command, Edmonton, Alta.; Saskatchewan—Dr. G. C. Bradley, 812 McCallum-Hill Bldg., Regina, Sask.; Manitoba—Dr. P. K. Tisdale, 501 Medical Arts Building, Winnipeg, Man.; Western Ontario—Dr. Berkley Brown, 325 Queen's Avenue, London, Ont.; Central Ontario—Lieut.-Col. A. E. Parks, 330 University Ave., Toronto, Ont.; Eastern Ontario—Lieut.-Col. John E. Baker, 520 College St., Kingston, Ont.; Western Quebec—Col. C. U. Letourneau, Queen Mary Veterans' Hospital, Montreal; Eastern Quebec—Major M. P. Simard, Hôpital des Anciens Combattants, Quebec; New Brunswick—Lieut.-Col. J. A. Melanson, Department of Health, Fredericton, N.B.; Nova Scotia—Surg. Comdr. C. M. Harlow, 98 Clarence St., Halifax, N.S.; Prince Edward Island—Lieut.-Col. R. D. MacNeill, Box 130, Charlottetown, P.E.I.

A branch for Newfoundland is presently under consideration.

The Second Pan American Congress on Pædiatrics will be held in Mexico City, November 2, 3 and 4, 1949. A very full program has been arranged. The following Canadian pædiatricians have been invited to read papers: Drs. D. B. Leitch, Alfred H. Spohn, A. W. Farmer and L. N. Silverthorne.

The Twelfth Annual Louis Gross Memorial Lecture, under the auspices of the Montreal Clinical Society, will be delivered at the Jewish General Hospital, Montreal, on Wednesday, October 26, 1949, at 8.30 p.m., by Dr. Louis N. Katz, Director of Cardiovascular Research—Michael Reese Hospital, Chicago, Ill., Professorial Lecturer in Physiology, Chicago University. The subject will be: "Clinical Electrocardiography—Its present position and possible potentialities".

The Royal College of Physicians and Surgeons of Canada. This year will mark the inaugural award of the annual prizes in Medicine and Surgery by the College. The awards are as follows: the Royal College of Physicians of Canada Medal was won by Dr. W. Stanley Harteroft of Toronto for his work on "Aspects of Experimental Choline Deficiency", and the Royal College of Surgeons of Canada Medal was won by Dr. Euchariste Samson, of Quebec, for his work on "Traitement Radical du Cancer de la Tête du Pancreas". These medals will be presented at the Annual Meeting of the College in November in Toronto.

The class of 1924 Medicine, University of Toronto, is holding its 25th Anniversary Reunion in Toronto, October 27, 28, and 29, in order to take in the Medical Alumni Refresher Course at Sunnybrook Hospital, the University of Toronto home-coming week-end, the Western-Varsity football game and their class dinner at the Royal York Hotel on October 29. The registration to date will make this the largest 2T4 Meds reunion ever held.

The fourth annual refresher course in general practice sponsored by the Medical Alumni Association of the University of Toronto will be held on October 27, 28, and 29, at Sunnybrook Hospital in Toronto. A varied and interesting program has been arranged. There is no fee, and all members of the profession are invited to attend.

Book Reviews

Crime and the Mind. W. Bromberg, formerly Director, Psychiatric Clinic, Court of General Sessions, New York. 219 pp. $5.50. J. B. Lippincott Co., Montreal, 1948.

The literature on psychiatric criminology is so vast that one is apprehensive in opening a new book on the subject. This apprehension is not justified in the present case. Dr. Walter Bromberg who writes out of an experience of many years as psychiatrist associated with the Court of General Sessions in New York is able to offer a comprehensive survey of the subject which is more than a mere repetition of what is known. This note of freshness and spontaneity is produced by the fact that the author draws on his personal experiences and on a description of cases rather than on psychopathological theory. As far as the latter is concerned he succeeds in integrating a sound psychoanalytical approach with the traditional approach of "school psychiatry". There are some weaknesses, *e.g.*, in the historical chapter the author omits the great psychologists of the humanist period, such as Vives, and gives the impression that the rational approach to the subject had been inaugurated at the time of the French Revolution. However, taking the book as a whole and a survey of its factual contents, it should be regarded as indispensable for anyone working in the field of criminology.

Dictionary of Genetics. R. L. Knight, Senior Economic Geneticist, Empire Cotton Growing Corporation and Sudan Government. 183 pp. $4.50. Chronica Botanica Co., Waltham, Mass.; Thorburn and Abbott, Ltd., Ottawa, 1948.

The science of genetics has developed in an amazing way in the last few years, and one evidence of this is the enormous number of new terms which have been coined to meet new needs. It is indispensable that special books should come into circulation constantly to reflect the state of knowledge on the frontier of research so that

students may follow developments and investigators have instruments to explore new territory. As sciences grow they form intercrescences with ancillary sciences, as genetics has with biochemistry and physiology, to mention only two. This means that workers in these fields must have ready means of correlating their thinking with that of geneticists. A good dictionary is of aid in all these ways. This one has 183 well printed pages on which the terms have been set in black-face type for ready reference. The binding is good. The definitions are concise and for the most part clear; but not always absolutely explicit, as that for "acquired character" which might be made to cover quite another thing such as malunion of a fracture. One finds hosts of current terms, new and old, such as heterochromatin, iso-alleles, line breeding, meiosis, mutation, nidation and sex hormones which have been gleaned from many fields, central and peripheral, in the great range of modern genetics. While tending to consolidate good new terms it tends, unfortunately, to establish some perhaps faulty, such as adaptive radiation where implications in physics might be avoided, perhaps, by the use of the word "divergence". The pitfalls besetting the way of the lexicologist are skimmed in the preface. As a specialist reference book this volume will be found useful where the ordinary medical dictionary, or the glossaries in the backs of genetics texts, would prove inadequate. Nine valuable appendices are here, on such subjects as chi, correlation coefficient, genotypes expected in backcrosses and in F_2s, International Rules for Symbolizing genes and chromosome aberrations, and others. It is to be hoped that physicians and medical students will purchase it and master its contents, for genetics has much to give them if they will but accept it. Genetics specialists and workers in related fields will find it invaluable.

Energetics of Human Behaviour. G. L. Freeman, formerly Professor of Psychology and Director of the Laboratory of Psychophysiology in Northwestern University. 344 pp. $3.50. Cornell University Press, Ithaca, New York, 1948.

This book is an extreme exponent of a behaviorist type of "psychology". The reviewer is purposely using quotation marks because in his opinion such books deal with a large number of things except one—the "psyche". Some people, looking at the extraordinary success of the natural sciences in the past hundred years, feel that it is just about time that something "objective" and quantifiable ought to be established in the sciences occupied with the human mind. They forget that here we find ourselves in an area in which the subjective is just as valid as the objective. When the physician is confronted with a problem of emotional suffering he will, whether he wants it or not, "put himself into" the patient, in other words, he uses the method of empathy, of re-experience. The behaviorist considers such procedure as "unscientific" because it cannot be reduced to formulæ and graphs. Thus, he regards only those aspects of "psychology" as scientific which can be quantified, and therefore, without admitting it either to himself or to others, has to be confined to the physiology of human behaviour. Of this approach the present book is an extreme representative. A physician may just have read one of the classical analyses of life histories as given by anyone of our great medical psychologists, or he may have listened to the grief of a bereaved relative, and then, on opening the present book he comes across a passage in which the human organism is compared to the mechanism of a motor car.

But man is essentially different from a machine. In a machine we can *explain* disturbances; in man we cannot only explain them but also *understand* them. This means that when we are facing, let us say, a murderer, we approach his problem as Shakespeare approached Macbeth's problem, *i.e.*, with the method of human understanding. To know something about Macbeth's frontal lobe, hypothalamus and suprarenal cortex will never give us a glimpse of the insight which we have when we look with psychologist Shakespeare at the *whole man*. Contrary to a combustion engine, man lives in a world of values and of freedom. Books like the present one would be valuable if they confined themselves to the discussion of the *physiology* of emotions, motility, etc. However, in claiming to replace other forms of psychology, such as psychoanalysis, phenomenology and gestalt psychology they forfeit their purpose. Moreover, in order to stress their scientific approach authors of books like this develop a "lingo" which conveys the impression of objectivity but actually serves to obscure comparatively simple common sense observations. Schopenhauser once said that all genuine and truly new ideas have the earmarks of being able to be expressed in a simple and clear language. This should be a warning for those among us who are so humble to think that because something sounds obscure it must be ingenious.

Radiology Physics. J. K. Robertson, Professor of Physics, Queen's University, Kingston. 323 pp., illust., 2nd ed. $2.50. D. Van Nostrand Co., Inc., Toronto, 1948.

This second edition contains all the good features of the first edition. The newer work on atomic physics, which has taken place since the first edition, is well covered in a clear and comprehensive manner. Dr. Robertson has the happy faculty of explaining complex physical phenomena in a simple yet clear and concise manner, which is understandable to those not possessing detailed knowledge of physics, and the subject matter is presented in a progressive developmental manner, which makes for very easy reading.

This book is ideally suited for doctors doing postgraduate study in radiology, for medical students, for x-ray technicians, and, indeed, for all medical men who wish to keep abreast of developments in medical radiation physics.

Renal Origin of Hypertension. H. Goldblatt, Director, Institute for Medical Research, Cedars of Lebanon Hospital, Los Angeles, Calif. 126 pp., illust. $4.00. Charles C. Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1948.

This is one of the series of American Lectures in Pathology. The author is Professor Harry Goldblatt and probably no one is in a better position or has a stronger right to speak with authority on the subject to which the lecture is devoted. His work in experimental hypertension has been so striking that in any informed discussion of the question the contributions he has made will be ignored only by the malicious. That the kidney is involved in essential human hypertension even in the early stage seems now to be incontrovertibly proved by the results obtained in animal experimentation. During the two decades of this experimentation physiologists, pathologists and pharmacologists have participated and the work has been carried on with reassuring precision and thoroughness. In seeking the genesis of essential human hypertension the attack on the kidney has been conducted as an orderly, relentless siege rather than in the form of daring, but sporadic, assaults and every gain was consolidated as the attack went forward. Thus the existence and the effect of renin, hypertensin, hypertensinogen and hypertensinase were gradually brought within the domain of accepted knowledge where they have an apparently indisputable permanence, and though progress was rarely dramatic it was always steady and impressive. It is the more important details of that progress which have been compressed into this relatively short lecture.

To say that the lecture is compressed is to make merely a comment and not a criticism. The style is straightforward and the meaning is seldom obscure, but the reasoning is so compact that it will not be readily followed by those who are entirely unfamiliar with the nature of the problem for which the solution was being sought. Laboratory workers will find the monograph a useful review and some knowledge of its contents is

obligatory for all consulting physicians and for many general surgeons. Through a careful reading of this little book the general practitioner will be better able to assay the merits of remedies proffered him for the management of patients who have hypertension.

Skin Diseases. A Manual for Practitioners and Students. J. Marshall, Consulting Dermatologist, Central Middlesex County Hospital. 363 pp., illust. $7.50. Macmillan & Co. Ltd., London and Toronto. 1948.

This small text should prove useful to the busy practitioner since it gives a bird's-eye view of the more frequently seen dermatoses. The author has given only the highlights in his descriptions, and his advice for therapy is perhaps a little too conservative. He stresses one point throughout, *i.e.*, use only bland applications. The chapter on Diagnosis is especially good and contains several anatomical sketches showing the distribution in various diseases. The author has thoughtfully inserted a short chapter on psychosomatic eruptions; this should spur the reader on to a closer survey of his dermatological patient's emotional status. The section on syphilis is well written and brief. In all this book is well illustrated and is a good elementary text for students and practitioners.

Synopsis of Physiology. A. R. Short, late Professor of Surgery, University of Bristol; C. L. G. Pratt, Lecturer in Mammalian Physiology, University of Cambridge; and C. C. N. Vass, Reader in Physiology in the University of London. 346 pp., illust., 4th ed. $5.00. John Wright & Sons Ltd., Bristol; Macmillan Co. of Canada Ltd., Toronto, 1948.

This summary of human physiology is prepared as a means of rapid revision for students and practitioners, and as a memory aid to lecturers. It cannot stand by itself as a text, nor is this the intention of the authors. Its purpose is, in general, well carried out. The general physician would find more value in a less abbreviated text unless his general knowledge of physiology is above average.

Principles and Practice of Ophthalmic Surgery. E. B. Spaeth, Professor of Ophthalmology in the Graduate School of Medicine of the University of Pennsylvania, Philadelphia. 1044 pp., illust., 4th ed. $16.90. Lea & Febiger, Philadelphia; Macmillan Co. of Canada, Toronto, 1948.

This is the fourth edition of a book which is authoritative, informative, and popular enough to be considered a classic. The author has brought his text up to date with several additions. These represent new knowledge based on war experience in the handling of eye injuries. The most notable change is in the chapter dealing with enucleation, where the new work on plastic implants has been included. In such a fine book it is perhaps lèse-majesté to say that the reviewer wishes the author had emphasized his own preferences a little more when discussing various operative techniques. However, this must not be considered in any way a criticism. Indeed, this valuable book can be mentioned only with praise.

Surgeon's Guide to Local Anæsthesia. C. E. Corlette, Consulting Surgeon, Sydney Hospital. 355 pp., illust. $7.50. John Wright & Sons Ltd., Bristol; Macmillan Co. of Canada Ltd., Toronto, 1948.

The first hundred pages of this book are taken up with a description of apparatus, local anæsthetic materials and the anatomy of the nervous system. The rest is given over to the description of the administration of local anæsthetics in various operative procedures. The field covered in such few pages is practically the whole surgical field from surgery of the head to surgery of the limbs. The value of this book to the practice of surgery in Canada is open to question. Anæsthetics are described under different names than those in common use here and this is confusing. During the last war, great advances were made in various forms of anæsthesia, spinal, intravenous and also in basal and general anæsthesia, which has certainly narrowed the field for local and regional administration to very exceptional cases. We have always felt that local anæsthesia was a personally perfected service. For this reason, it has never come into widespread use. This little book might be of use as a short quick review of the use of local anæsthesia in various operative procedures.

Principles and Practice of Rectal Surgery. W. B. Gabriel, Surgeon to St. Mark's Hospital for Cancer, Fistula for Cancer, Fistula and Other Diseases of the Rectum. 508 pp., illust., 4th ed. 45s. H. K. Lewis & Co. Ltd., London, 1948.

The fact that this volume has run into four editions since its publication speaks for its popularity. It is a very useful book, both for the proctologist and the general practitioner, containing definite instructions on what to do and how to do it. Few surgeons on this side of the Atlantic would, however, agree with the author on the long stay in bed after hæmorrhoidectomy. A new chapter on incontinence is very interesting.

Diseases of the Ear, Nose and Throat. D. G. Carruthers, Honorary Ear, Nose and Throat Surgeon, Sydney Hospital and Eastern Suburbs Hospital, Sydney. 344 pp., illust., 2nd ed. $6.25. John Wright & Sons Ltd., Bristol; Macmillan Co. of Canada Ltd., Toronto, 1948.

This is an excellent book—not cluttered up by a rehash from old textbooks and well worth having. The operation for removal of tonsils and adenoids is well described by both the guillotine and dissection methods. The word "guillotine" might well be discarded as the modern instrument is a far cry from the original, due to the simultaneous work of Sluder of St. Louis and Willis and Pybus of Newcastle. Allergy is rightly stressed, as also is dermatitis of the external ear, not overlooking fungus infections. Penicillin and the use of sulfonamides are included. In cases of otosclerosis, the fenestration operation is scarcely given due credit. It is the only real approach to this condition that has ever been made.

Recent Advances in Surgery. H. C. Edwards, Surgeon and Lecturer in Surgery, King's College Hospital, London. 437 pp., illust., 3rd ed. The Blakiston Co., Philadelphia, 1948.

This is a British publication originally compiled by Sir Heneage Ogilvie and now carried on by Mr. Edwards in the recent edition. Its purpose is to supplement established surgical texts by a periodic coverage of the new developments in surgery. Three of the sections are written by other prominent London surgeons, a point which adds to the effectiveness of this volume. The combined authors have moulded their sections from their own experience, knowledge accruing from the recent war, and from outstanding articles appearing in the international literature. A bibliography of these articles appears at the end of each section. Much of the information offered is of necessity somewhat abbreviated in such a small volume, and the criticism can be levelled that this book is neither "fish, flesh, fowl or good red herring" but the reader will be well repaid especially in the sections on the alimentary tract, blood vessel surgery and that concerning radiotherapy in malignant disease. In general it can be said that the authors' object has been successfully achieved in producing a surgical supplement of recent advances, especially useful for the surgeon who is not in constant contact with a medical centre and who has not the time to keep abreast of the main surgical periodicals.

Recent Advances in Cardiology. T. East, Physician, and Physician-in-charge of Cardiological Department, King's College Hospital; and C. Bain, Physician, Harrogate General Hospital. 454 pp.,, illust., 4th ed. The Blakiston Co., Philadelphia and Toronto, 1948.

This text presents an up-to-date review of cardiovascular disease in a remarkably concise well-ordered manner. The material has been selected with great care while, if one wishes to pursue a subject or a statement further, excellent references have been tabulated. The approach has been an essentially clinical one with greater emphasis on diagnosis and treatment. The grouping of some of the diseases seems a little strange at first but it may facilitate the brevity of the review. Congenital defects have been classified on a developmental basis which, although more logical, is less practical and more confusing to the clinician. On the whole, however, this is a very readable little book which should be useful to both the student and practitioner.

Essentials of Pathology. L. W. Smith, formerly Professor of Pathology, Temple University School of Medicine; and E. S. Gault, Associate Professor of Pathology and Bacteriology, Temple University School of Medicine. 778 pp., illust., 3rd ed. The Blakiston Co., Philadelphia and Toronto, 1948.

The third edition of this now well-recognized textbook of Pathology has been extensively revised with new material and illustrations added. It is remarkably up-to-date with recent knowledge for a standard textbook. The general arrangement of this book follows a traditional pattern with 328 pages devoted to general pathology, 392 to systemic pathology and 21 to a bibliography. A distinctive and interesting feature is the presentation of brief illustrative case reports in all sections, including the anatomical and microscopic pathology. This serves as a correlation between clinical and pathological features. A few unfortunate statements are noted, such as the one on page 451, where, in relation to carcinoids of the intestine, it is said that they behave in similar benign fashion to those of the appendix. In figure 169 the word Oroya is misspelled, and the legends for figures 185 and 186 are reversed. One would have no hesitation in highly recommending this book to medical students or as a reference book for general medical usage.

Elementary Anæsthesia. W. N. Kemp, Consultant Anæsthetist, Children's Hospital, Vancouver. 289 pp., illust. $5.00. The Williams & Wilkins Co., Baltimore, Md.; The University of Toronto Press, Toronto, 1948.

As the title implies, the author claims that the book is written for undergraduate students and general practitioners. The good basic references are mixed with the author's bizarre collection of ideas. It is hardly advisable, especially to students, to stress in italics that "the safety of chloroform lies in its depth", or that ethyl chloride is a very useful agent to be used as frequently as the author suggests. The outlined management of vomiting and aspiration during anæsthesia is antiquated. Oxygen, the most important agent in the resuscitation of the newborn is advocated only after the old series of shock-producing measures are listed. With the intratracheal catheter method of resuscitation the operator is not warned that the infant's lungs may easily be ruptured with much positive pressure. Carbon dioxide absorption is not as efficient as the author suggests, especially in pædiatric anæsthesia, and the patient may build up large depressing amounts of carbon dioxide. Throughout the book, there is no stress laid on the vital importance of oxygen, a bag, and mask being readily available when starting any anæsthetic.

It is concluded, that while the book contains a good series of references and illustrations, it is certainly no handbook for the beginner.

Blood Transfusion. E. L. DeGowin, Associate Professor of Internal Medicine, State University of Iowa; R. C. Hardin, Assistant Professor of Internal Medicine, State University of Iowa; and J. B. Alsever, Senior Surgeon, U. S. Public Health Service. 587 pp., illust. $10.00. W. B. Saunders Co., Philadelphia and London; McAinsh & Co. Ltd., Toronto, 1949.

This very excellent book covers the entire field of the transfusion of blood, its derivatives and substitutes. The short historical perspective in the first chapter deals principally with the modern application of blood transfusion since the revelation of the major cause of fatalities in this practice by the discovery of the four blood groups at the turn of the century. The introduction in 1914 of sodium citrate as an anticoagulant, the discovery of methods of preservation of blood two years later, the demonstration of pyrogens in 1923, the use of plasma and its fractions and finally, the discovery in 1940 of the Rh factors and isosensitization, have provided technical procedures that make practical the transfusion of safe blood and its derivatives.

Here in Canada with the institution of the nation-wide Red Cross Blood Transfusion Service still more safe blood will be used. Before accepting this freely-flowing blood, it behooves everyone prescribing it to make himself familiar with the indications for the kind and amount required lest there be waste and the safety of the patient be jeopardized. By injudicious use or carelessness, "safe" blood can be made unsafe. As the authors remark "blood transfusion cannot be carried out as simply as in the good old days". After all, they are not so old. This business of blood transfusion has become rapidly a complicated affair even though an abundance of it and a simple apparatus for its administration be put into our hands. This book provides an excellent guide for the transfusionist and the blood banker in the use of this great life saving procedure.

Atlas of Neuropathology. Wm. Blackwood, Assistant Pathologist, The National Hospital, Queen Square, London; T. C. Dodds, Laboratory Supervisor, Department of Pathology, University of Edinburgh; and J. C. Sommerville, Senior Technician, the Department of Neuropathology, University of Edinburgh and Scottish Mental Hospitals' Laboratory. 199 pp., illust. $8.75. E. & S. Livingstone Ltd., Edinburgh; Macmillan Co. of Canada Ltd., Toronto, 1949.

This book undertakes to illustrate the typical gross and microscopical appearances of intracranial lesions and it fulfils its purpose admirably. The pathological specimens shown and adequately described are those encountered with reasonable frequency in a neuropathological laboratory. Photographs of normal structures are placed beside the pathological specimens where they are helpful. Due emphasis is given to the important subject of mechanical displacements of the brain in trauma and in cases with space-occupying lesions. The illustrations are excellent throughout. Colour has been used where it is of value. Modern staining methods have been used very effectively to demonstrate specific microscopical features. This volume will be of great value for general laboratory use and particularly, as the authors say, in the hands of clinicians and of pathologists beginning the study of neuropathology.

Diseases of the Adrenals. L. J. Soffer, Associate Attending Physician, The Mount Sinai Hospital, New York City. 320 pp., illust., 2nd ed. $6.75. Lea & Febiger, Philadelphia; Macmillan Co. of Canada Ltd., Toronto, 1948.

The great advances which have been made in the general study of endocrinology in recent years have made it difficult for the non-specialist to keep pace with the newer diagnostic methods and treatment. In this book, Soffer has presented what is known about the adrenal cortex and medulla in a clear, usable form. The normal

anatomy and physiology of the gland are presented as background from which he works to presenting symptoms, differential diagnosis and treatment of the various disorders of the adrenal. The disease patterns are presented clearly and are well illustrated. There is a complete outline of laboratory methods for the diagnosis of adrenal cortical disease in which the methods for estimating blood electrolyte values might perhaps be more up to date, but elsewhere the material is as new and complete as can be expected in such a rapidly developing field.

Aviation Medicine in its Preventive Aspects. J. F. Fulton, Sterling Professor of Physiology, Yale University. 175 pp., illust. $3.50. Oxford University Press, New York, 1948.

This small volume is composed of the Heath-Clark Lectures (1947) delivered at the London School of Hygiene and Tropical Medicine. It is essentially an historical review from the time of Robert Bayle to the present. It is divided into five parts which deal with the history of oxygen and altitude sickness and acclimatization; the genesis of the tissue bubble and decompression sickness; the spring of the air and pressure cabins and explosive decompression; protective measures; and man and the machine. In this short space a broad panorama of the essential foundations of aviation medicine is outlined in a clear and most entertaining manner. Every student of this subject should have a copy of this book not only for itself but also for the excellent source bibliography which it contains.

Diseases of the Nose and Throat. Sir St.Clair Thomson, Officer de la légion d'Honneur; Commander (with Swords) of the Order of Leopold of Belgium; fellow of King's College, London, and V. E. Negus, Surgeon for diseases of the Throat, Nose and Ear, King's College Hospital. 1004 pp., illust., 5th ed. $16.00. Appleton-Century-Crofts, Inc., New York, 1949.

Shortly before his death in 1943, Sir St.Clair Thomson began this fifth edition. It was completed by his colleague and collaborator, Mr. V. E. Negus, who perpetuates and brings to modernity this classical English text. Few parts of the book have escaped alteration, much has been added but a considerable amount has been reduced, for instance the description of atrophic rhinitis and syphilis. Welcome additions are the chapters on allergy, the sulfonamides, penicillin and other antibiotics and the use of radiotherapy in the treatment of nasal conditions. Part VI on diseases of the pharynx and tonsil is good and complete, embracing the subject from detailed and well-illustrated methods of tonsillectomy to the problems of pharyngeal diverticulæ and the neurologic disorders of the pharynx. Equally good are the chapters on the larynx and peroral endoscopy, the trachea, bronchi and œsophagus where the able hand of Mr. Negus is again apparent. It is recommended to the medical profession as easy to read and well worth its price.

Introduction to Gastro-Enterology. W. C. Alvarez, Professor of Medicine, University of Minnesota, The Mayo Foundation. 925 pp., illust., 4th ed. $12.50. Paul B. Hoeber, Inc., New York, 1948.

The general practitioner will not wish to read this book from cover to cover. However, the enquiring one will enjoy the reading of various chapters on such subjects as the motor functions of the small bowel, the gradient theory, vomiting, gas in the bowel, constipation and a complete review of vagotomy. The correlation of animal experimental work, human physiological studies and the clinical observations of the bedside or office practice are found in this book. It abounds in information that is difficult to find elsewhere. The physiologist, as well as the physician and surgeon who has a particular interest in the digestive tract will find this an indispensable book. Some will not agree with a number of Dr. Alvarez's hypotheses to account for some intestinal symptoms and signs. However, all will agree that in this book is collected an unusually complete knowledge of intestinal function. The fact that Dr. Alvarez stresses our deficiency of knowledge by posing more questions than he attempts to answer makes this a stimulating volume. The author's interest in medical history adds to the value of the book. This is a "must" for students of this subject as well as medical libraries.

Blakiston's New Gould Medical Dictionary. Edited by H. W. Jones, Honour Graduate, Army Medical School; N. L. Hoerr, Henry Willson Payne Professor of Anatomy, School of Medicine, Western Reserve University, Cleveland; A. Osol, Professor of Chemistry and Director of the Chemistry Department, Philadelphia College of Pharmacy and Science, Philadelphia, Pennsylvania; with the cooperation of an Editorial Board and 80 contributors. 1294 pp., illust. $8.50. The Blakiston Company, Philadelphia and Toronto; Doubleday Publishers, Toronto, 1949.

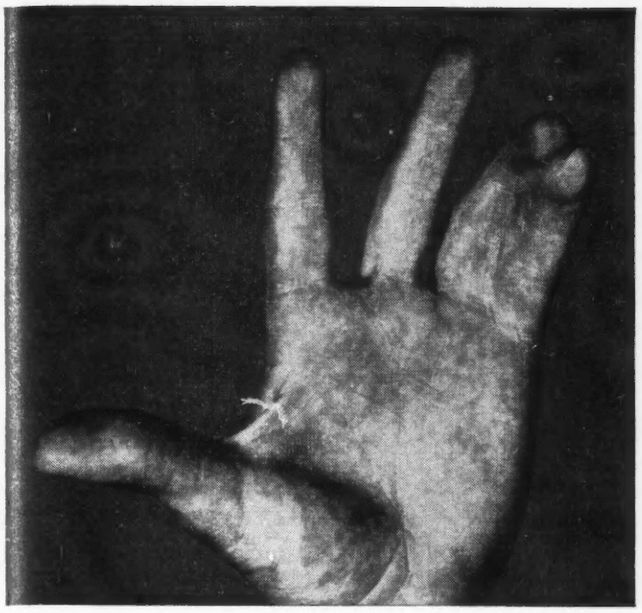
The name of Gould has been long associated with medical lexicography. The present however is by far the most ambitious version which has appeared under his name and actually is completely new. It has been produced by three editors, an editorial board and 80 contributors, and embraces terms used not only in medicine and allied sciences, such as dentistry and nursing, but also in veterinary medicine, zoology and botany. This is very convenient. The definitions are concise and accurate, and the type is bold and well spaced. Illustrations have been brought together in one section and are well done. The book is an important addition to medical lexicography and should prove popular.

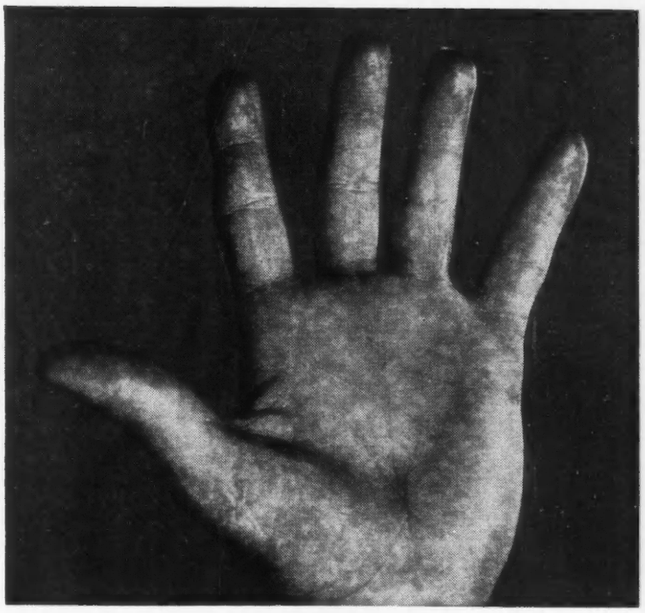
Critical Studies in Neurology. F. M. R. Walshe, Fellow of the Royal College of Physicians, London. 256 pp., illust. $3.75. E. & S. Livingstone Ltd., Edinburgh; Macmillan Co. of Canada Ltd., Toronto, 1948.

This small volume is a collection of papers by a most distinguished neurologist which have previously appeared in *Brain*. The papers for the most part are critical studies of some of the more recent physiological theories of concepts which have evolved regarding the nervous system.

Lung Dust Lesions (Pneumoconiosis) versus Tuberculosis. L. G. Cole. 474 pp., illust. $10.00. American Medical Films, Inc., White Plains, N.Y., 1948.

This book contains detailed descriptions of the author's and his son's studies in the field of the pneumoconioses studies which have been carried on over a period of many years. After presenting the problem of the differentiation of lung dust lesions and tuberculosis, as he sees it, the author proceeds to describe methods which he has found useful in the anatomical recognition of these lesions. He has found the collagen content and the presence or absence of birefringent particle invaluable aids in the anatomical differentiation of lesions due to dusts and to tubercle bacilli. Following this he describes Delafield's classification of tuberculosis and presents data indicating that he considers Delafield's terminology useful in the classification of both tuberculous lesions and lesions resulting from the inhalation of dust. He then describes the roentgenological findings in cases of tuberculosis and in cases of silico-tuberculosis. The conclusion appears to be that lesions due to dusts and lesions due to tubercle bacilli cannot, in many instances, be differentiated on roentgenographic findings alone. This book is written in a conversational and, at times, argumentative style. It contains an unusually large number of reproductions of photographs of lesions as seen at necropsy examination as well as of chest roentgenograms of persons known to have or believed to have pneumoconioses or tuberculosis, or both.





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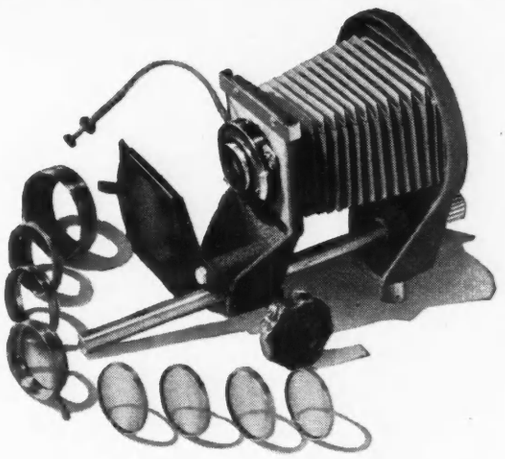

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Clinical Aspects and Treatment of Surgical Infections. F. L. Meleney, Associate Professor of Clinical Surgery, College of Physicians and Surgeons, Columbia University. 840 pp., illust. $13.00. W. B. Saunders Co., Philadelphia and London; McAinsh & Co. Ltd., Toronto, 1949.

This is a book that is likely to be consulted as a final authority on surgical infections until new discoveries make the sulfonamides and antibiotics obsolete. It is the fruit of 36 years of intensive work that began in Zinsser's laboratory and was continued in the surgical wards of the Presbyterian Hospital, New York. Some of the material on streptococcal infections was found in China when the author served a term in the Peking Union Medical College. The greater part is gleaned from the records of the department of surgery in the Columbia Presbyterian Medical Centre over a period of twenty-five years. The advent of chemotherapy and penicillin intensified the researches of the author and a group of men who studied with him. One result was the discovery of the antibiotic bacitracin.

Infections in every organ of the body are separately considered and illustrative case reports prove, if proof were needed, that the book is no compilation but the result of painstaking study.

It was in Meleney's own laboratory that the cause of undermining burrowing ulcers, hæmolytic streptococcal and progressive bacterial synergistic gangrene was established. There, too, valuable work was done on the science of prescribing antibiotics. But this is not a work on bacteriology. It is a study of infections in every organ of the body by a skilled surgeon who bases his treatment on that which he has learned in the laboratory. Case histories illustrate every conclusion drawn. Techniques are not dogmatically detailed but the indications for operation are clearly given and the rational procedures stated in terms that any surgeon can follow. Every surgeon, tyro or veteran, can find profit in reading this book. Teachers of surgery will find it invaluable.

Primary Anatomy. H. A. Cates, Professor of Anatomy, University of Toronto. 478 pp., illust. $6.00. The Williams & Wilkins Co., Baltimore; The University of Toronto Press, Toronto, 1948.

A solution of the perennial problem of teaching basic anatomy to groups who have little or no background of scientific knowledge is here attempted by Dr. Cates. The author begins with a discussion of the cell, traces the organization of cells into tissues and then the subsequent specialization of these latter into systems. From that point the treatment of each system proceeds, beginning in each instance with general principles in order to show how each system is adapted to the tasks it must perform. The student is thus not required to memorize so much as to understand. Dr. Cates has a fine flair for clear writing and a happy facility of choosing good examples to fortify his points. In addition, his medical background enables him to choose and stress those facts which are of clinical importance rather than treating the subject academically. The illustrations are clear, ample and excellent. On the whole, this book should be most helpful for anatomical teaching in the ancillary fields of Medicine.

Child Psychiatry. L. Kanner, Associate Professor of Psychiatry, The Johns Hopkins University. 752 pp., 2nd ed. $10.50. Charles C. Thomas, Springfield, Illinois; The Ryerson Press, Toronto, 1948.

It is a rare pleasure for a reviewer to have the opportunity to read such an excellent book. This second edition is not a mere revision of the first edition, which had five printings, but a complete rewriting. The material covered is far greater, the presentation is less burdened by psychiatric terminology and treatment is more fully described, and the bibliography is very adequate. This book, a classic in its field, is highly recommended not only to medical students and pædiatricians, but to all physicians who treat children and their parents. The author does not present a theory to account for aberrations in children's behaviour; the reader is not confronted with sibling rivalry, or castration fear, or masturbation guilt as the cause of problem children. Instead, the author describes the "common sense" approach (which is, in this book, really common sense) to sick children, sick parents and troublesome environments. Also, this book is an excellent reference book for answers to the questions of many parents about their children. Finally, it has great value as a basic text for the interpersonal problems of all people, not only children.

Introduction to Cardiology. G. Bourne, Physician, and Physician in Charge of the Cardiological Department, St. Bartholomew's Hospital. 264 pp., illust. $4.50. Edward Arnold & Co., London; Macmillan Co. of Canada, Toronto, 1949.

This book is an outstanding example of a good book produced by a good teacher. It was a pleasure for this reviewer to notice how beautifully Dr. Bourne draws on his store of knowledge to generalize and synopsize so that the important facts stand out clearly and simply. He makes no attempt to show how clever he is, rather he is concerned with teaching the non-specialist a useful amount of cardiology without delving into the more esoteric elements of the subject. The book is, wisely, very brief so that it requires no great amount of time from either the student or busy practitioner, yet every chapter rewards the reader richly. The stress throughout is upon the clinical history and physical examination of the patient with thorough guidance through the maze of special examinations. The entire book aims to show the general practitioner how much more he can do rather than leaving him with the feeling that even the simplest problem requires the aid of a specialist. This is an excellent, useful manual.

Surgical Pathology. P. A. Herbut, Professor of Pathology, Jefferson Medical College, Philadelphia, Pennsylvania. 710 pp., illust. $13.50. Lea & Febiger, Philadelphia; Macmillan Co. of Canada Ltd., Toronto, 1948.

This book has been written to cover the surgical pathology of the major surgical operations—ear, nose and throat, urology, gynæcology and general surgery. Naturally in a book of this length there are many gaps; but the more common and important conditions are included. There is a short, but concise account of the embryology, anatomy and histology of each system, which is extremely useful in the interpretation of pathological lesions and saves the reader the necessity of referring to a separate text. A certain amount of clinical information is included and the accepted form of treatment is briefly mentioned when indicated. The book is well illustrated with photographs and photomicrographs and there is a comprehensive and up-to-date bibliography for each section. It is a book of considerable value to the student, intern and postgraduate student, as well as the practising surgeon.

The Frontal Lobes. Proceedings of the Association for Research in Nervous and Mental Disease, December 12 and 13, 1947, New York. Vol. 27, 901 pp., illust. $12.50. The Williams & Wilkins Co., Baltimore, 1948.

This important volume represents the proceedings of the 27th meeting of the Association for Research in Nervous and Mental Diseases. A timely and important subject is presented. The volume includes papers presented by many authorities in the different aspects of frontal lobe. Part One discusses the biology of the frontal lobes. Part Two represents experimental work that has been done. Part Three is clinical studies in the frontal lobe and Part Four is a review of important work done on frontal lobotomy. For neurologists and psychiatrists who are interested in frontal lobotomy as a treatment in certain forms of mental diseases, this book will provide a very important addition to their library.

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Recent Advances in Respiratory Tuberculosis. F. Heaf, Senior Medical Officer, London County Council; and N. L. Rusby, Assistant Physician, The London Hospital. 290 pp., illust., 4th ed. J. & A. Churchill Ltd., London; The Blakiston Co., Philadelphia and Toronto, 1948.

This book follows the style of previous editions. Accounts of developments which have taken place since the 3rd Edition of this volume was published in 1937 have, for the most part, been engrafted upon a background of previously-held ideas and concepts. A few new chapters on environment and social circumstances as they affect measures for the prevention and control of tuberculosis have been introduced. This edition, like former editions, contains many statistical summaries and detailed descriptions of procedures used to control tuberculosis. Among the latter are to be found descriptions of radiological equipment and methods used in the detection and treatment of persons with pulmonary tuberculosis, descriptions of methods—including the laryngeal swab technique—of searching for tubercle bacilli, and descriptions of therapeutic pneumoperitoneum and extra fascial apicolysis with thoracoplasty. Rehabilitation—including village settlements, special workshops and certain financial arrangements designed to aid in the rehabilitation of the tuberculous which have been introduced in England in recent years—is also discussed in some detail. One additional feature deserves special comment. This is the fact that the authors have seemingly had access to the published reports of an unusually large number of western European and Scandinavian observers. As a result of this, the references which are to be found at the ends of the chapters constitute valuable source material.

Obstretic Analgesia and Anæsthesia. F. F. Snyder, Associate Professor of Obstetrics and Associate Professor of Anatomy, Harvard Medical School. 401 pp., illust. $7.25. W. B. Saunders Co., Philadelphia and London; McAinsh & Co. Ltd., Toronto, 1949.

Here is something new and different for both the obstetrician and the anæsthetist. The bock is a well written, comprehensive review with excellent summaries of each chapter. It is divided into two sections: (1) Respiratory Injuries of the Child. (2) The Treatment of Pain During Labour. The former presents experimental and clinical evidence for the latest concepts of fetal respiration, intrauterine pneumonia, fetal atelectasis and asphyxia. The latter section, of practical significance to the anæsthetist, discusses the most widely used analgesic and anæsthetic drugs with some interesting and new highlights, *viz.*, the respiratory rate of the fetus is a good index of narcosis; bradycardia (rate below 100) is evidence of fetal anoxia and tachycardia (rate 160+) denotes recovery from a period of anoxia; full surgical anæsthesia of the mother may be obtained with cyclopropane without interruption of fetal respiration; the complication of labour and the misuse of analgesic drugs are more important causes of fetal asphyxia than nitrous oxide, ethylene, and cyclopropane; the danger of regional anæsthesia to the fetus lies in the severe anoxia produced by a small drop in maternal blood pressure.

Surgery of the Hand. S. Bunnell, Honorary Member of Academy of Orthopædic Surgeons. 930 pp., illust., 2nd ed. $18.00. J. B. Lippincott Co., Philadelphia, London and Montreal, 1948.

This edition is some two hundred pages longer than its predecessor and is much more profusely illustrated. Apart from the introduction of several new and ingenious reconstructive procedures, the essential superiority of this edition over the first lies in the fact that the author has been able to assess from his unprecedented vantage point during the war, the value of various types of treatment and of various reconstructive procedures. Full advantage has been taken of this vast experience in the present edition.

In the chapter on Dupuytren's contracture, Volkmann's ischæmic contracture, etc., an interesting, newly recognized entity — fibrous contracture of the intrinsic muscles of the hand is described. The prophylaxis and the treatment of the condition in its incipient stages is described together with an ingenious reconstructive procedure for the relief of the condition when fully developed. This latter comprises subperiosteal lengthening of the interossei if they are active or tenotomies if they are fibrosed beyond repair.

The section on the correction of bony deformities is extremely comprehensive and presents many new metacarpal reconstructions including the extremely useful metacarpal "jogging" for the relief of fingers which cross in flexion due to the loss of support of the head of a central metacarpal. The surgical repair of the small joints of the hand is fully described together with the use of occupational therapy, physiotherapy and other methods of rehabilitation.

The sections dealing with acute hand injuries, vasomotor and trophic disturbances, congenital anomalies and tumours maintain the high standard of the earlier chapters. The subject matter here though is more or less common knowledge whereas the sections on reconstruction of the crippled hand are crowded with recent advances in the critical appreciation of the nature of the lesions and with ingenious procedures designed for their amelioration. Since its first appearance this authoritative and comprehensive book has evoked the universal praise of surgeons. The advances in this recently developed and difficult field of surgery which have been made by the author and his associates whom he has trained and inspired are incalculable. The book should be read and kept as a reference by everyone concerned in the treatment of injured and crippled hands.

Practical Orthoptics in the Treatment of Squint. T. Keith Lyle, Surgeon and Medical Officer in charge of Orthoptic Department at the Westminster branch of the Moorfields, Westminster and Central Eye Hospital, King's College Hospital, and Sylvia Jackson, formerly Senior Orthoptist, Royal Westminster Ophthalmic Hospital. 271 pp., Ill., 3rd ed. 35s. H. K. Lewis & Co. Ltd., London, 1949.

In this third edition, the material has been completely worked over and brought up to date. Every chapter shows these changes. However, the basic treatment of the original material has not been altered. This text is most deservedly a standard one. It is a "must" for student orthoptist and ophthalmologist alike. The subject, which in many ways is still controversial, has been handled in a most sane, comprehensive, and readable way. In keeping with the title, the book is intensely practical. Nonetheless, the reviewer has certain criticisms to make which diminish his praise somewhat, but still must not be considered telling enough to destroy the book's great merit. The chapter on Heterophoria is by far the weakest. The problem of the selection of patients with heterophoria for orthoptic treatment is admittedly a most difficult one. Its complexities have been much too briefly handled. Further, the discussion of the methods used for testing ocular muscle balance is something less than critical. In discussing the Bishop Harman diaphragm test, some mention is made of the details of how to measure the interpupillary distance. Much more is required, as the accuracy of this test depends upon the exactness of this measurement. In Canada at least, this is one of those simple things that is so often poorly done. One is surprised at the authors making this statement on p. xii in reference to heterophoria in the R.A.F.; "Many pilots who would otherwise have been 'grounded' were enabled to return to full flying duties as a result of efficient orthoptic treatment". Let us hope this statement does not mean what it seems to say. There is ample evidence, quite available to the authors, that under the conditions of flying in the

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last war heterophoria had little if any influence on the ability to fly. The failure to mention this work, points up another criticism. The book would have had much more value for the close student, and much more authority, if references had been supplied. Such are used all too sparingly.

Value of Hormones in General Practice. W. N. Kemp. 115 pp. Burgess Publishing Co., Minneapolis, Minn.

This manual has been prepared with the expressed purpose of assisting general practitioners in the utilization of the many pharmaceutical hormonal preparations now available. The treatment of the subject is brief and to the point. The physiological background of each gland is presented briefly and followed by an outline of disease processes and treatment. While the material thus presented can be valuable information for the practitioner it is doubtful whether, in the present state of our knowledge of endocrinology, the subject lends itself to such summary treatment. The therapy of many of the conditions described is hardly so cut and dried as a perusal of this text implies. It is the opinion of this reviewer, for example, that it is not wise to base a decision to administer testosterone to a hypogonadal patient with only the physical examination as basis for separating pituitary from testicular dysfunction. Similarly, it does not appear proved that the thiourea preparations are entirely adequate therapy in hyperthyroidism. Perhaps the author might well have rounded out this presentation by placing more stress upon contraindications and hazards.

Textbook of the Rheumatic Diseases. Edited by W. S. C. Copeman, Physician to the Rheumatism Department and Lecturer in the Medical School, West London Hospital, London. 612 pp., illust. $12.50. E. & S. Livingstone Ltd., Edinburgh; Macmillan Co. of Canada, Toronto, 1948.

This book is published primarily on account of an increasing interest in the rheumatic diseases and because in October, 1946, at a meeting of the Empire Rheumatism Council, Sir Wilson Jameson, the Chief Medical Officer of the Ministry, stated that the British Government now regarded the campaign against rheumatism as one of the big tasks that they must face. It is the British counterpart of the American textbook, *Arthritis and Allied Conditions* by the late Bernard I. Comroe.

Any textbook that is written by one person usually has certain consecutive and correlated advantages and the modern tendency towards collaboration for more complete objective knowledge loses something in readability. This seems applicable to the book under review. Also the British point of view in rheumatism is very strongly influenced by the physiatrist, whereas in North America the physician or internist is primarily concerned with so-called rheumatism as regards etiology and treatment; and uses as an aid the physiatrist in a similar manner to the roentgenologist or radiologist. In the textbook under review there are 30 chapters and 24 contributors, consequently overlapping is inevitable. Some chapters are particularly good and some rather cursory and incomplete. The clinical classification of the Rheumatic Diseases is simple and workable. It is a welcome relief to note the inclusion of the term non-articular rheumatism and that less emphasis has been laid on the much abused one, fibrositis. Unfortunately there is very little reference to the recent work on the study of collagenous factors which is exciting so much interest on this continent.

This book can be recommended safely to the student and practitioner especially interested in rheumatic disease but it seems to the reviewer it should be paired with Comroe's *Arthritis and Allied Conditions*, as one is complementary to the other.

Neoplasms of Bone. B. L. Coley, Attending Surgeon, Bone Tumour Department, Memorial Hospital for Cancer and Allied Diseases. 765 pp., illust. $17.50. Paul B. Hoeber Incorporated, New York, 1949.

This book contains a wealth of information arranged in a most practical way. As the author states, it is designed for the use of not only the oncologist, but of the general practitioner, the internist, the surgeon, the orthopædist and the radiologist. The consulting pathologist will also find it most useful. However, the book is concerned chiefly with the clinical and radiological, rather than the pathological, aspects of the subject, yet there is sufficient pathology, accompanied by many good illustrations of gross and histological lesions, to give the clinician a good understanding of the nature of the diseases under discussion.

One often hears the statement that bone tumours are not important because they are not common; that the serious malignant ones are even less common and are hopeless anyway. This defeatist attitude is to be deplored. It is true that malignant bone tumours are uncommon compared with all other forms of malignant tumours. Yet when they are encountered they seem more tragic because of the fact that most of them occur in the adolescent or young adult. Their importance is just that of any other malignant tumour and the responsibility of the physician is not lessened because they are uncommon. The author points out that the majority of cases come to treatment after they have been present in a detectable stage for five or six months. The plea is made for earlier diagnosis and more prompt and adequate treatment as it is reasonable to expect thereby that more favourable results will be obtained. The doctor who first sees the case should insist upon an adequate and, if needs be, repeated expert radiological examination. No less important is the distinction between benign and malignant lesions so that unnecessary mutilating operations shall not be performed, or that the correct diagnosis shall not be postponed. This book makes available a most valuable experience from a rich source of material over a period of twenty-five years.

Coronary Artery Disease. E. P. Boas, Associate Physician, Mount Sinai Hospital, New York City; and N. F. Boas. 399 pp., illust. $6.00. Year Book Publishers, Inc., Chicago, 1949.

It is not often that the ideals stated by an author in his preface are so closely approximated as in this book. Dr. Boas has stated "the book is designed as a useful tool for the practising physician, but the presentation is sufficiently detailed to make it of interest to the cardiologist as well". He achieves just that and has, in addition produced a most readable text. The salient features regarding the anatomy, embryology and physiology of the coronary vessels are presented first. Here the teacher emerges, for the detail which is not yet integrated with the clinical picture is stripped away, leaving a clear description. On this solid foundation a scheme of the pathogenesis of coronary artery disease is erected in which the life span of the individual is the reference frame. The reader is thoroughly impressed with the fact that the patient with coronary insufficiency or with a frank myocardial infarct is seeking consultation at one point in the evolution of his disease and it is the individual rather than the disease which must be treated.

The differential diagnosis of coronary artery disease with or without infarction is not handled like a railway time-table. Those conditions which might be confusing are presented one at a time and interpreted functionally wherever possible so that differentiation is based only on considered reason not upon the retention of a series of isolated facts. The book, like the patient, reaches the climactic point of the life history of coronary artery disease in the episode of infarction, then considers the sequelæ and special aspects of treatment. This book can be highly recommended.